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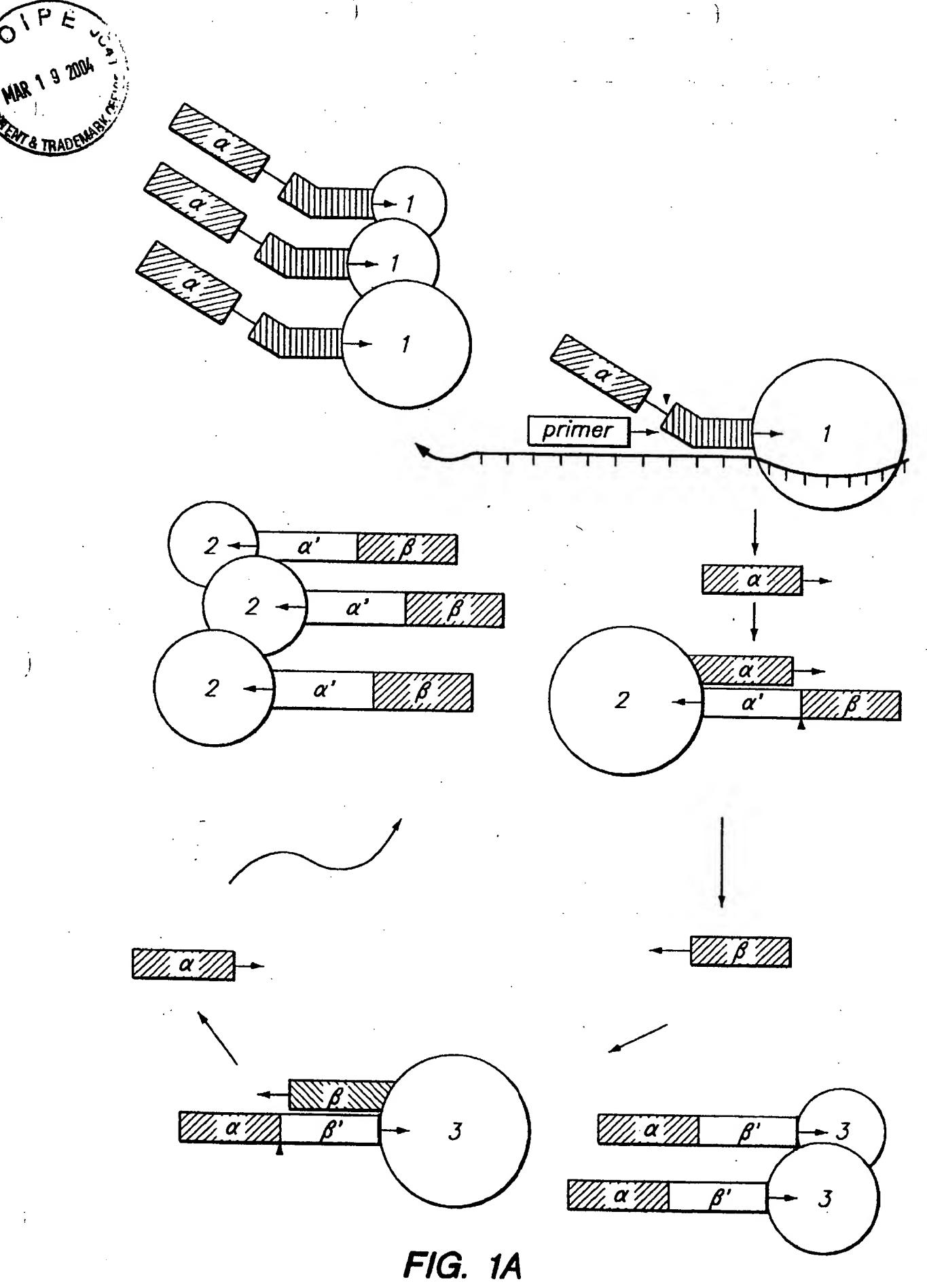
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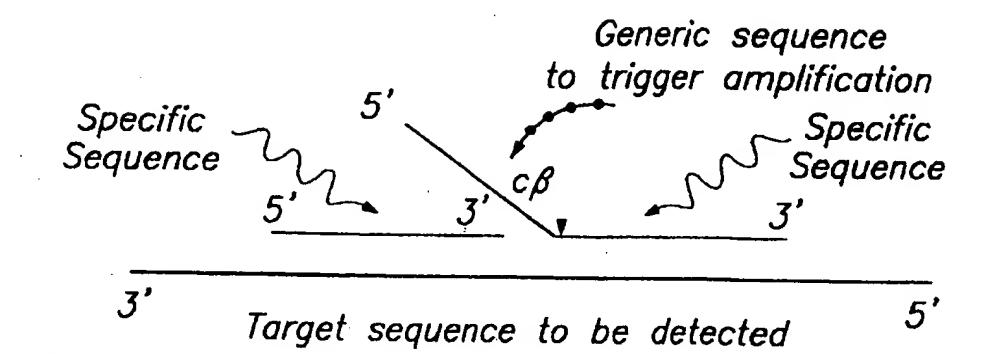
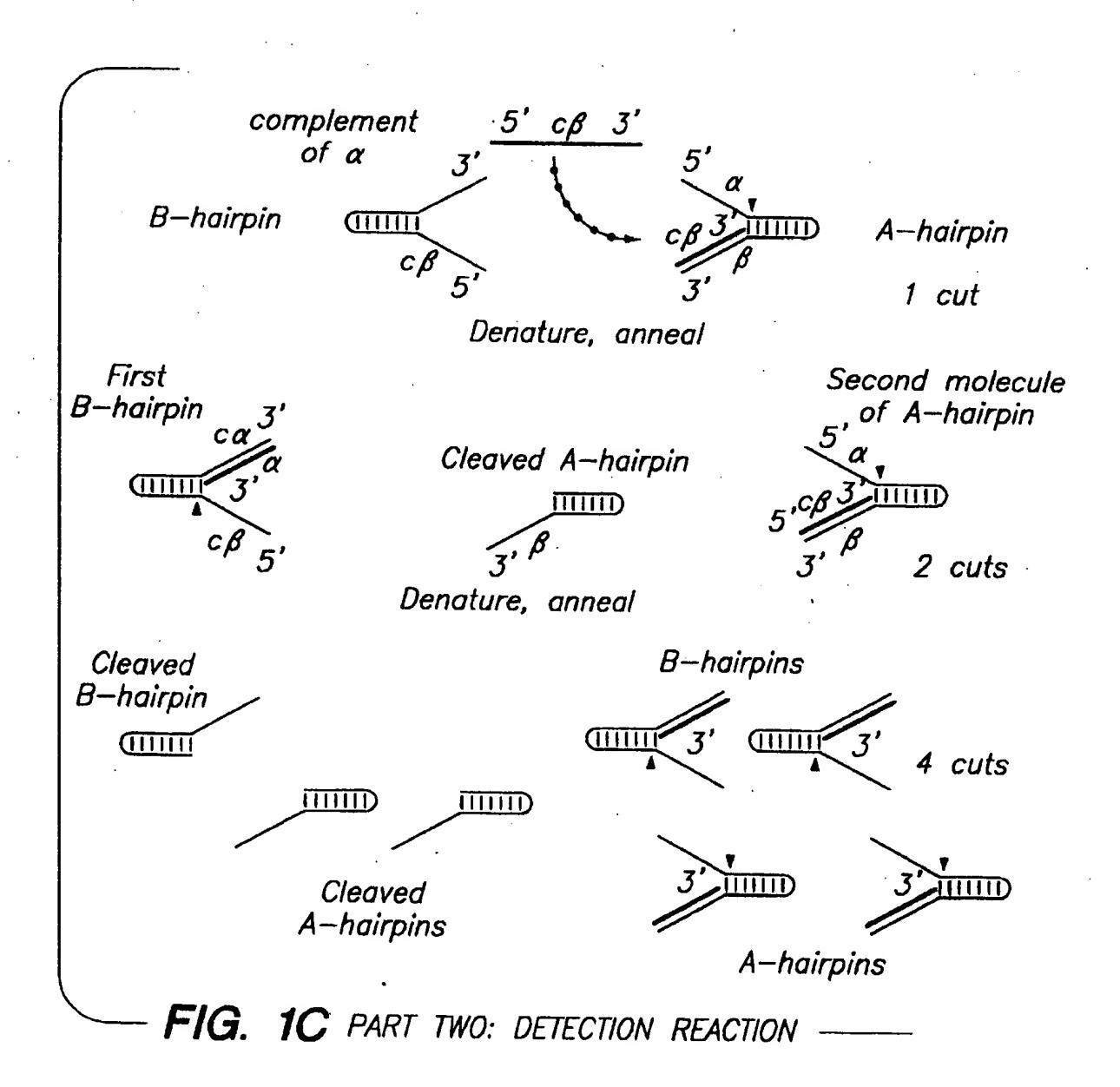


FIG. 1B PART ONE: TRIGGER REACTION





## FIG. 2A

MAJORITY	r esec id no:73	AT GXX GGCGAT GCTT CCCCT STTT SAGCCCCAAGGCCGGGCT CCT CCT GGT GGGCGCCACCACCT GGCCT	
DHAPTAG BHAPTFL BHAPTTR	ESED 10 NO: 17 ESED 10 NO: 23 ESED 10 NO: 33	. AG. G	57 57 70
	MAJORITY	A CC & CA & COTT COTT CO COT CACCA CCA CC	
	DRAPTAO DRAPTFL DRAPTTE	• • •	140 137 140
	MAJORITY	CGCCAAGAGCT CCT CAAGGCCCT GAAGGAGGACGGGGACXXGGGGGGT GXT CGT GGT CTTT GACGCCAAG	
	DNAPTAO DNAPTFL DNAPTTN	67. T. 67. T	207 204 210
	MAJORITY	G C C C C C C C T C C G C C C C C C C C	
	DRAPTAO DNAPTFL DNAPTTH		277 274 280
	MAJORITY	CCCGCCAGCT CGCCCT CAT CAAGGAGCT GGT CGT CCT CCT GGGGGTT GCGCGCCT.CGAGGT CCCGGGTA	
	DNAPTAO DNAPTFL DNAPTTB	G	347



## FIG. 2B

MAJORITY	CSEO ID NO:73	CBA B G C G G G G G G G C C C C C C C C C C	
DNAPTAG DNAPTFL GRAPTTR	ESEO 10 NO:13 ESEO 10 NO:23 ESEO 10 NO:33		417 414 420
	MAJORITY	A C C G C C G C G C G C C C C C C C C C	
	DRAPTAQ DRAPTFL DRAPTTR		487 484 490
	MAJORITY	T CACCCCGGCGT GGCTTT GGGABAGT ACGCCCT GAGGCCGGAGCAGT GOBT GGAGT ACCGGGCCCT GGC	
	DRAPTAO DRAPTFL DRAPTTB	G	557 554 560
	MAJORITY	GEGEGACCCCT CCGACACCT CCCCGGGGT CAAGGGCAT CGGGGAGAGACCCGCCCX GAAGCT CCT CXAG	
	DRAPTAQ DRAPTEL DRAPTTR	6	627 624 630
	MAJORITY	GAGT GGEGGAGCCT GGAAACCT CAAGAACCT GGACCGGGT GAAGCCCCCC CXT CCGGGA GAAGA	
	DRAPTAO DRAPTFL DRAPTTR	6 6	694 691 700



## FIG. 2C

ESEO ID NO:73	T CCA GG C C C A C C T C C T C C T C C T C C C C	
ESEC 10 NO:17 ESEC 10 NO:27 ESEC 10 NO:37	F	764 781 770
MAJORITY	GGT GGACTT GGCCAAGKGGGGGGGGGGGGGGGGGTTAGGGGCTTT CT GGAGGGGCT GGAGTTT	ŕ
DNAPTAO DNAPTFL DNAPTTH	66.6.6.6.0.4. A. T. 66. T. T. 6. T.	834 831 840
MAJORITY	GGCAGCCT CCT CCACGAGT T CGGCCT CCT GGAGGGCCCCCAAGGCCCT GGAGGGAGGCCCCT GGCCCCCT GGCCCCCGCC	٠
DNAPTAO DNAPTFL DNAPTTB	. А	904 901 910
MAJORITY	CGGAAGGGGCCTT CGT 8GGCTTT GJ CCTTT CCGGCCCCGAGCCCAT GT GGGCCGAGCTT CT GGCCCT GGC	
DRAPTAO DRAPTFL DRAPTTR	T. TT. T.	974 971 980
MAJORITY	CGCCGCCAGGGAGGGCCGGGTCCACCGGCCACCAGTTTAXGGGCCTXAGGGAGCTXAAGGAGGTG	
DNAPTAO DNAPTFL DNAPTTR	T. GG., GT, G., G., C., G., T. A., AA, G., G., G., G., G., G., G., G., G., G.	1044 1041 1050



#### FIG. 2D

MAJORITY	ESEQ ID NO:73	CGBGGKCT CCT GCCGAGGT GGCCGTT T T GGCCCTT GAGGGGCCCT XGACCT CXT GCCGGGGGGGG	
BRAPTAD DRAPTFL DRAPTTR	CSEO 10 NO: 17 CSEO 10 NO: 27 CSEO 10 NO: 27	G. T. G. T. G.	1114 11120
	MAJORITY	Accepat bet cet cecet a cet cet ce ce ce ce ce a ce	
	DNAPTEL		1184 1181 1190
	MAJORITY	GEGEGEAGT GEACGEAGEGEGEGEGEGECT CCTXT CCGAGAGECT CTT CCX GAACCTXXX GGAG	
	DRAPTAG DRAPTFL DRAPTTR	C	1254 1251 1260
	MAJORITY	CGCCTTGAGGGGGAGGGCTCCTTTGGCTTTACCAGGGGGGGAGAGCCCCTTTCCCGGGTCCTGG	
	DNAPTAO DNAPTFL DNAPTFL	A. B. A. A. A. A. A. B	1324 1321 1330
	MAJORITY	cceaeat goaggecarggest x ceect beacet gecet act ccaesecet xt ecct seabet becsea	
	DNAPTAO DNAPTFL DNAPTTR	66. C	1394 1391 1400



## FIG. 2E

EAJUELL 1	[SEG 10 NO.7]	GEAGAT CC6CC6CCT C6A66A66ACGT CTT CC6CCT G6CC6GCCA CCCCTT CAACT CAACT RCC6GAC	
DRAPTAO DRAPTFL DRAPTTR	[SEO 10 NO: 13 [SEO 10 NO: 23 [SEO 10 NO: 33]		
	MAJORITY	CAGET GEAAAGGET GET ETT CACCAGET X GGGET T CCCCCAT CGGCAAGA CGGAAGA CX GGCAAGC	ပ
	DNAPTAO DNAPTFL DNAPTTR	60. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 6. 6. 6. 1. 1. 1. 6. 6. 6. 1. 1. 1. 6. 6. 6. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.	153 153 154
	MAJORITY	BCT CCACCAGCGCCGCCGT GGAGGCCCT X CGX GAGGCCCACCCCAT CGT GGAGGAGAT CCT GCAGTA	æ
	DNAPTAO DNAPTFL DNAPTTH	G. C. C. G. B. G. C. C. G.	1604 1601 1610
	MAJORITY	CC G G G G G C C C C C A G C A C A C A C	/5
	DRAPTAG DRAPTFL DRAPTTR	6. A. C. C. C. C. A. C. A. C. A. C. A. C. A. C.	1674 1671 1680
	MAJORITY	C G C C T C C A C C C C C C A C C C C C C C	
	DRAPTAG DRAPTFL DRAPTTR		1744 1741 1750



#### FIG. 2F

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MAR 1.9 2004			1814 1811 1820		1884 1881 1890		1954 1951 1960		2024 2021 2030		2094 2091 2100	·	; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;
CHA TRADEMARY.	FIG. 2F	a gaa cat coccest coccest ceeccas cas gas cat cocces cocct t cet seccea seas sest		GT T GGT GGCCCT GGA CTATAGC CAGATAGA GCT CCG GGT CCT GGC CCA CCT CT CCGGGG CGA CGA CCT G	A	AT CCGGGT CTT CCAGGAGGGGGGGGACAT CCACACCCCAGGCGGCCAGCT GGAT GTT CGGCGT CCCCCGG		A GOCCOT GOACCECCT GAT GEGEGEGEGECCAAGEAT CAACT T CGGGGT CCT CT A CGGCAT GT EEG	A. G.G. A	CCACCECT CT CCCAGGAGCTT GCCAT CCCCTACGAGGGGGGGGT GCCCTT CATT GAGCGCTACTT CCAG	GG. T. TA. G. T. T. A. T. T. A. T. A		
		ESEC ID NO.73	ESEO 10 NO: 13 ESEO 10 NO: 23 ESEO 10 NO: 33	MAJORITY	DRAPTAQ DRAPTFL DRAPTTR	MAJORITY	DNAPTAO DNAPTFL DNAPTTH	MAJORITY	DRAPTAG DRAPTFL DRAPTTR	MAJORITY	DNAPTAO DNAPTFL DNAPTTH		
. ,		MAJORITY	DNAPTAO DNAPTFL DNAPTTH							•		•	



#### FIG. 2G

MAJORITY	ESED 10 NO.73	AGET T CCCCAAGGT GCGBGCCT GGAT T GAGAGCCCT GGAGGGGGGGGGGGGGGG	
DNAPTAG DNAPTEL DRAPTTE	ESEO 10 NO: 17 ESEO 10 NO: 27 ESEO 10 NO: 37		2164 2161 2170
	MAJORITY	CECT CTT CEGCCECCESCECT ACET ECCCGACCT CAACGCCCGGGT GAAGACGT GCGCGGGGCGCGGGGCGGG	
	DNAPTAO DNAPTFL DNAPTTR	G	2234 2231 2240
	MAJORITY		
	DNAPTAQ DNAPTFL DNAPTTR	93	2304 2301 2310
	MAJORITY	tt beecebbet X cabbaaat BBB beceabbat bet bet x cabbit ecabbabet bet bet bet be bebe	
	DNAPTAG DNAPTEL DNAPTTR	A	2374 2371 2380
	MAJORITY		
	DNAPTAQ DNAPTFL DNAPTTN		2444



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#### FIG. 3A

MAJORITY	r ESED 10 NO:83	MXAML PLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEPVQAVYGFAKSLLKALKEDG- DAVXVYFDAK	
TAO PRO TFL PRO TTR PRO	ESED ID NO:47 ESED ID NO:53 ESED ID NO:63		63 70
	MAJORITY	APSFRHEAYEAYKAGRAPTPE BFPROLALIKEL VOLLGL XRLEVPOYEABDVLATLAKKAEKE GYEVRIL	
	TAO PRO TFL PRO TTR PRO		138 140
	MAJORITY	TABROLYOLLSBRIAVLHPEGYLI TPAWLWEKYGLRPEOWVDYRALXGOPSONLPGVKGI GEKTAXKLLX	
	TAO PRO TEL PRO TER PRO		209 208 210
	MAJORITY	EWGSLENLLKNIDRVKP-XXREKIXAHMEDLXLSXXLSXVRTOLPLEVOFAXRREPDREGLRAFLERLEF	
	TAO PRO TFL PRO TTR PRO	A. FOH. Q. St. 10.6. A. A. RK. Q. H. GR. T. M. E. B. L. B. LE. B. L. O. G	278 277 280
	MAJORITY	GSLLHEFGLLEXPKALEEAPWPPPEGAFVGFVLSRPEPMWAELLALAAARXGRVHRAXDPLXGLRDLKEV	
	TAG PRO TFL PRO TTR PRO	S. S. K. B. K. B. G. WE. L. D. R. G. B. K. G. B. A. K. G.	348 347 350



#### FIG. 3B

MAJORITY	ESEO IO NO:83	RGLLAKOLAVLAL REGLOLXPGOOPMLLAYLLOPSNTTPEGVARRYGGEWTEDAGERALLSERLFXNLXX	
TAO PRO TFL PRO TTM PRO	[SEO ID NO: 4] [SEO ID NO: 5] [SEO ID NO: 6]	S 6. P A WG	418 417 420
	MAJORITY	RLEGEERLLWLYXEVEKPLSRVLAHMEATGVRLDVAYLOALSLEVAEEI RRLEEEVFRLAGHPFNLNSRD	
	TAG PRO TFL PRO TTR PRO	K. K. H. B.	488 487 490
	MAJORITY	OLERVLFDELGLPAIGKTEKTGKRSTSAAVLEALREAHPIVEKILOYRELTKLKHTYIDPLPXLVHPRTG	
	TAO PRO TFL PRO TTH PRO		558 557 560
	MAJORITY	RL HT RF NOT AT AT GRL SSSOP NL ONI PVRT PLGORI RRAF VAEE GWX L VAL DY SOI EL RVLAHL SGBENL	
	TAO PRO TFL PRO TTM PRO		628 627 630
	MAJORITY	I RVF DE GROI HT OT A SWAIF GV PPE A VOPL AR RAAKTI NF GVL Y GAIS AHRL SOEL AI PY E E AVAFIERYFO	٠
	TAG PRO TFL PRO TTR PRO	8. S. 6. S.	698 697 700



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MAR 1 9 DUNELLERY		768 757 87	833 835 835	
TRADELINE.	FIG. 3C Sfpkyrawiektleegrrbotlegrrypdinary	F P B L X E MG A B B		
	[S£0 id #0:8]	222 3	TAO PRO TFL PRO TTH PRO	· ·
	MA JORITY	•		



for Wild-Type and Pol(-)DNAPTag Genes

Polymerase 5' Nuclease Coding Regions: Domain FIG. 4A

Codons essential to polymerase (wt)

20 Pst 48 FIG. 4C FIG.

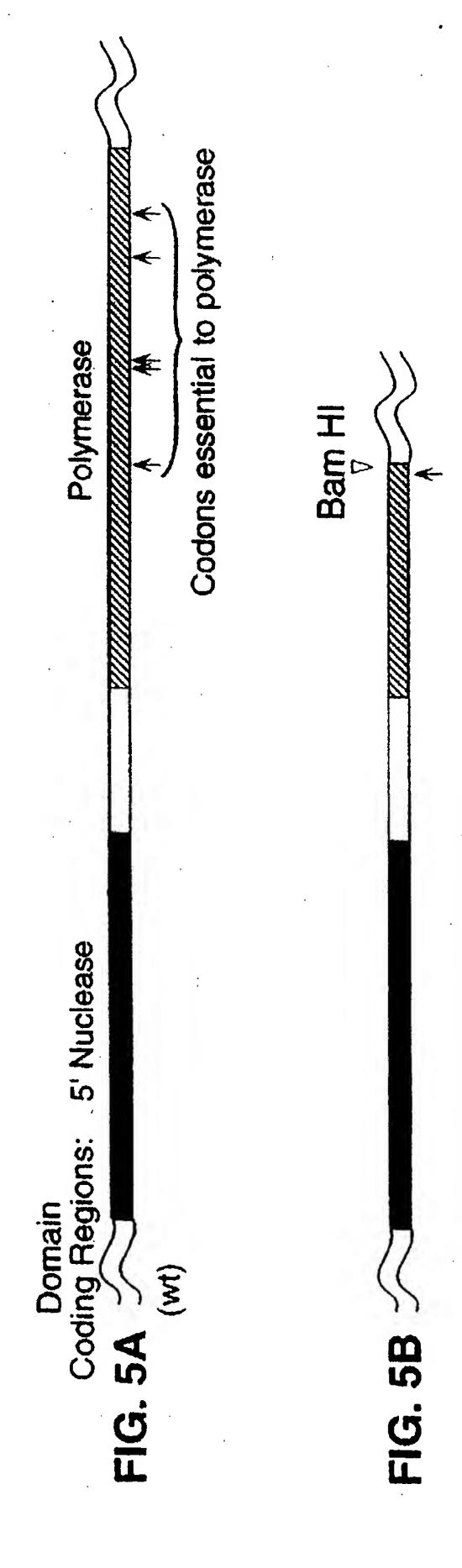
Whe I ...... FIG. 4D Xcm BstX / FIG. 4E

Bam Hi BstX 1 FIG. 4F

Not , TGA BstX / FIG. 4G



# Genes for Wild-Type and Pol(-) DNAPTfl



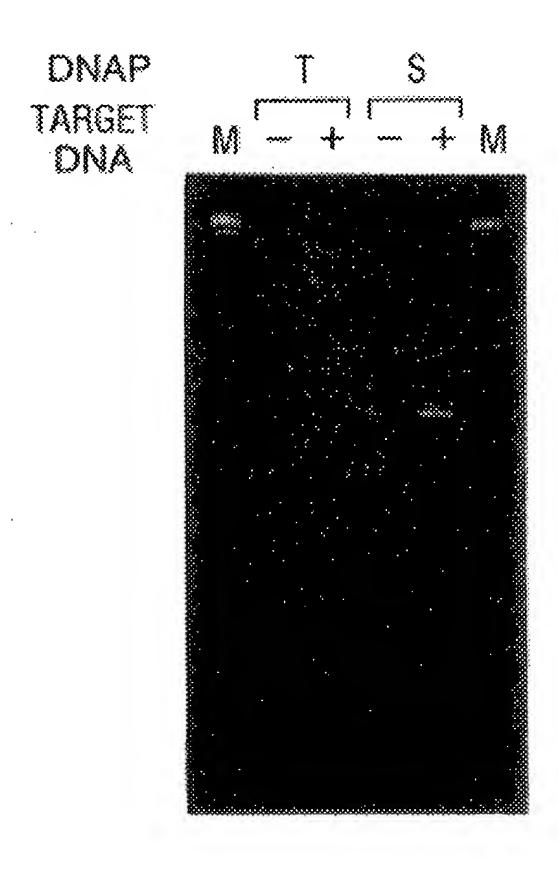
Substrate Strain.

Substrate Strain.

CGGAATTCGAGCTCGC

CGGAATTCGAGCGGG Template Strand Cleavage SANTAL CONTRACTOR OF THE CASE OF THE CONTRACTOR S STREET, WEST, STREET, STREET







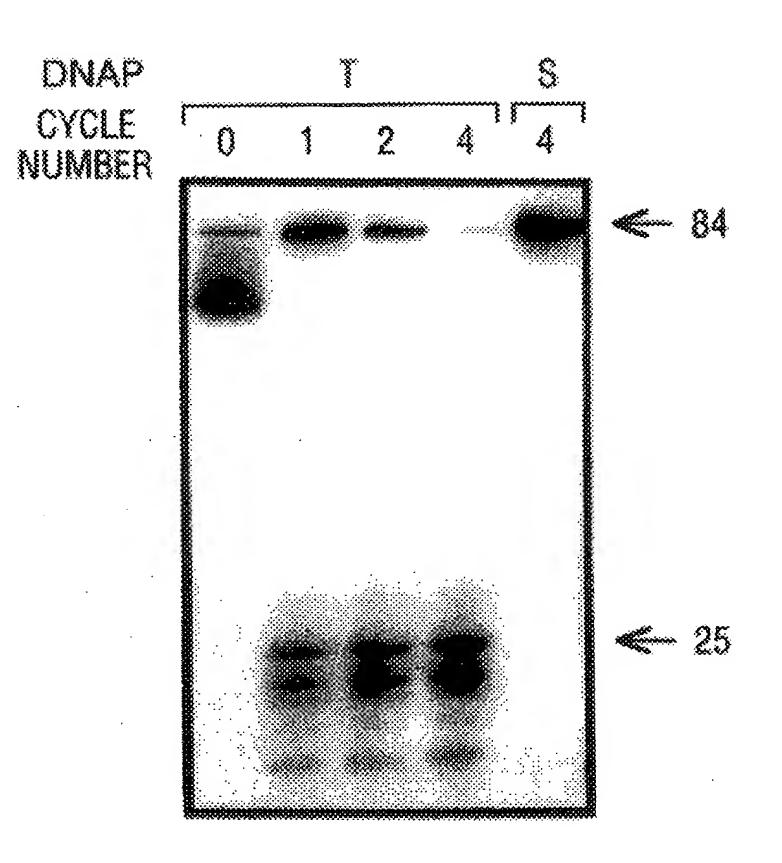


FIG. 8



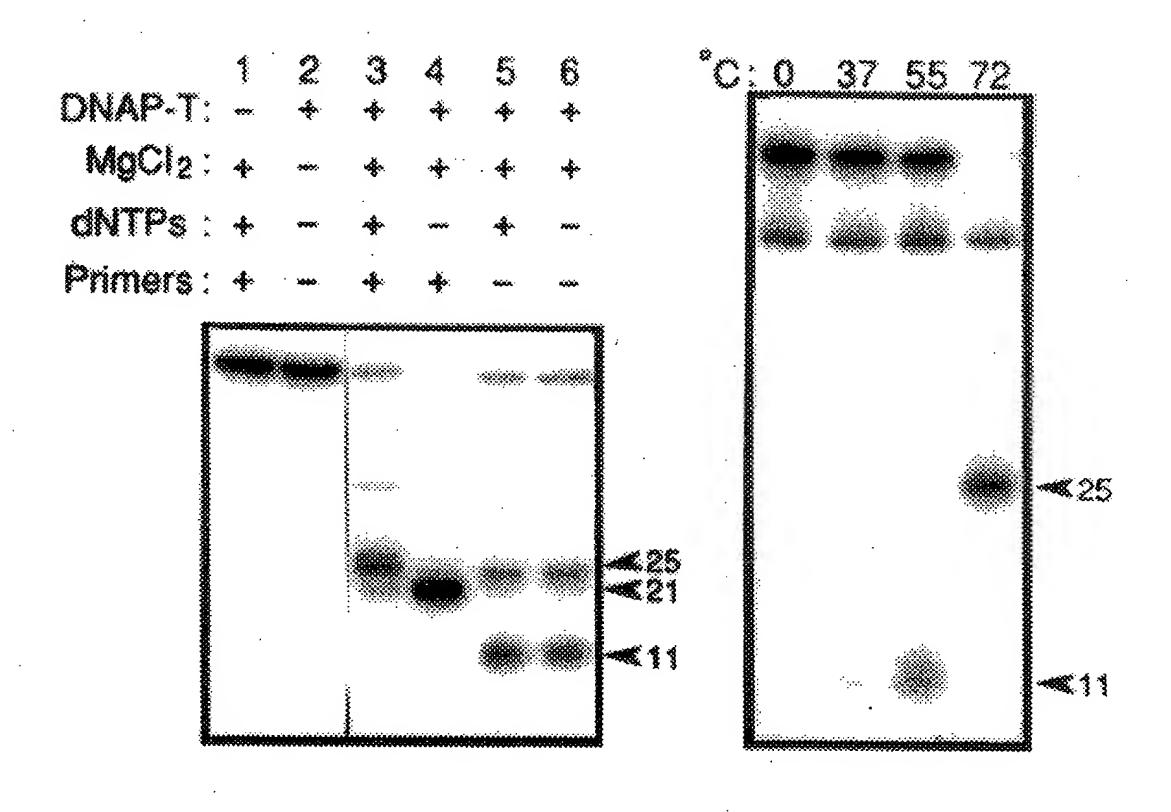


FIG. 9A

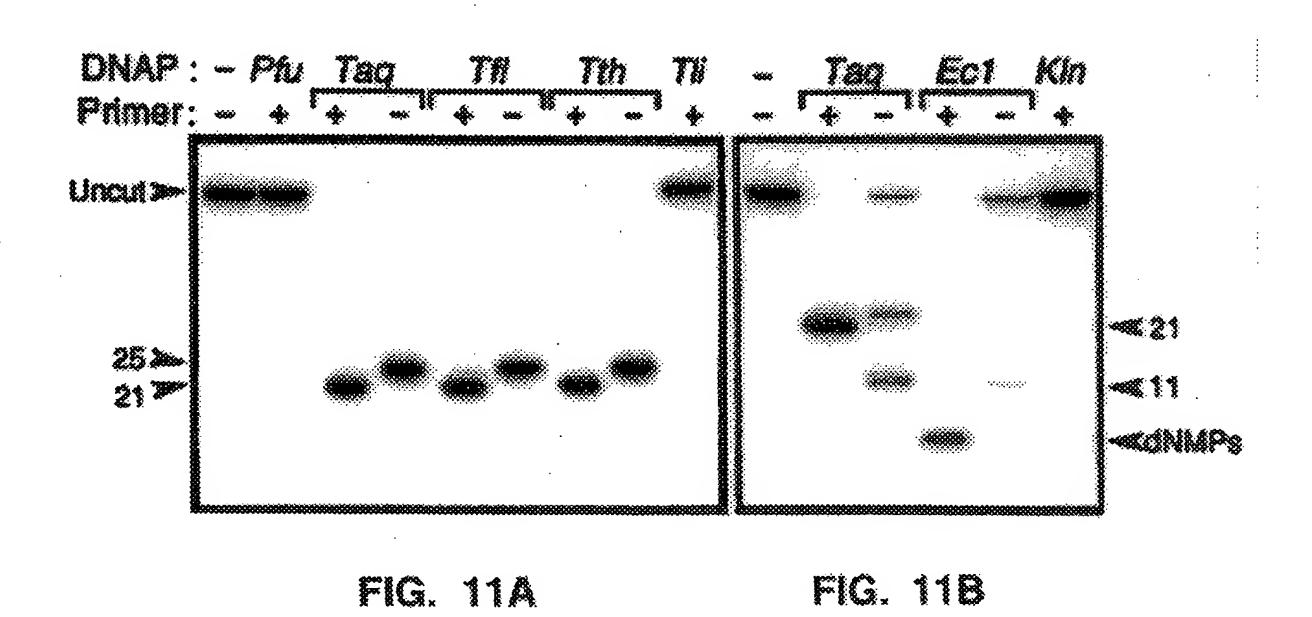
**\*\***C. **9**D



t (MIN): M 0 0.5 1 3 5 10 M M 0 5 10 20 40 60 M

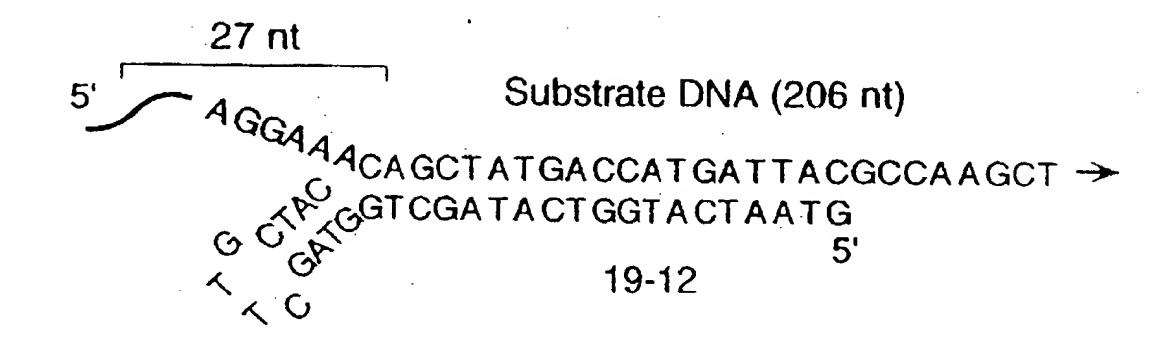
FIG. 10A

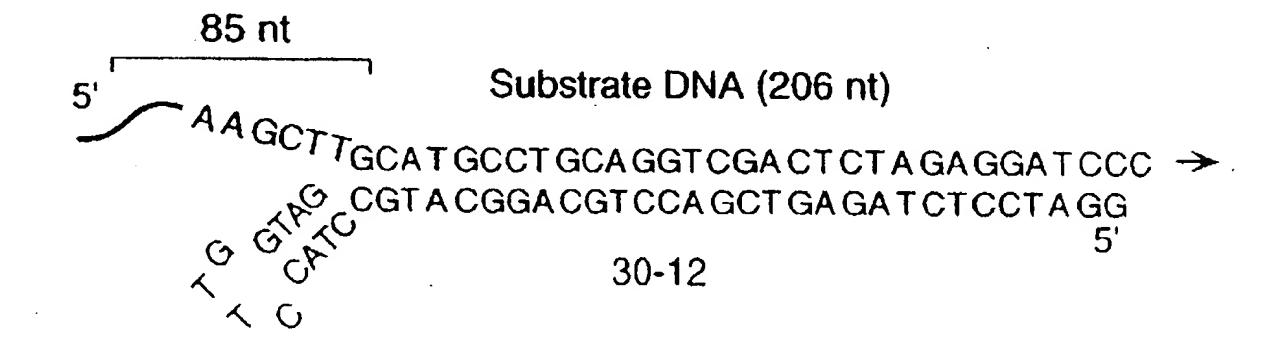
FIG. 108





#### FIG. 12A







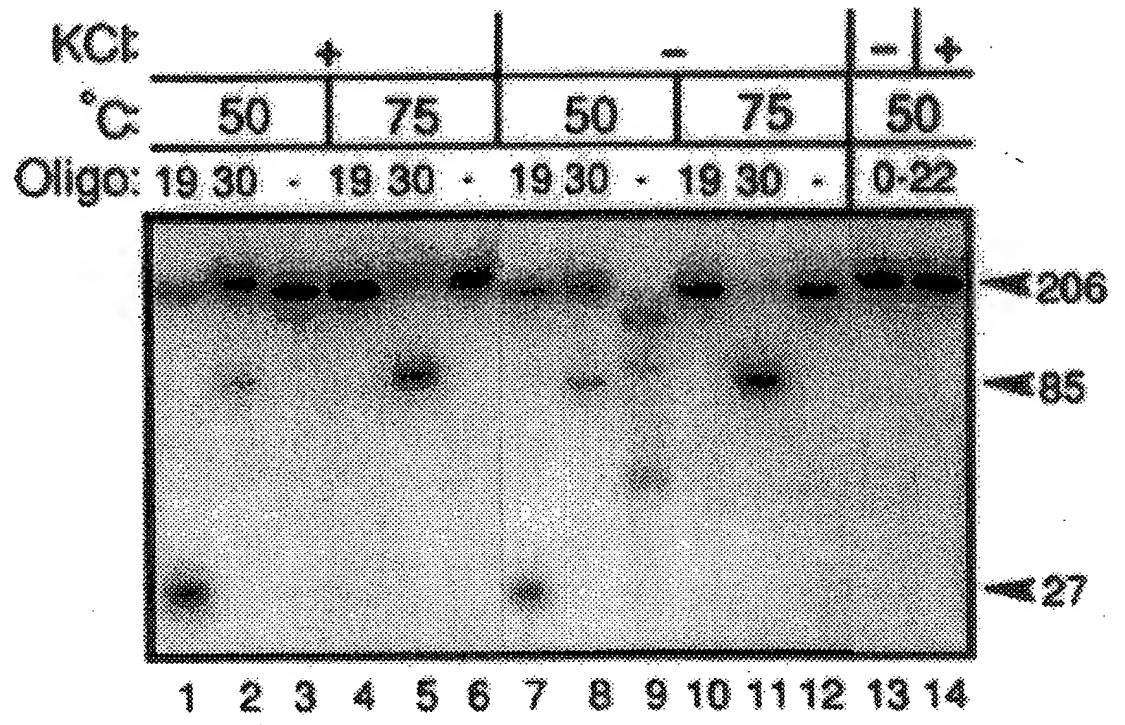


FIG. 120

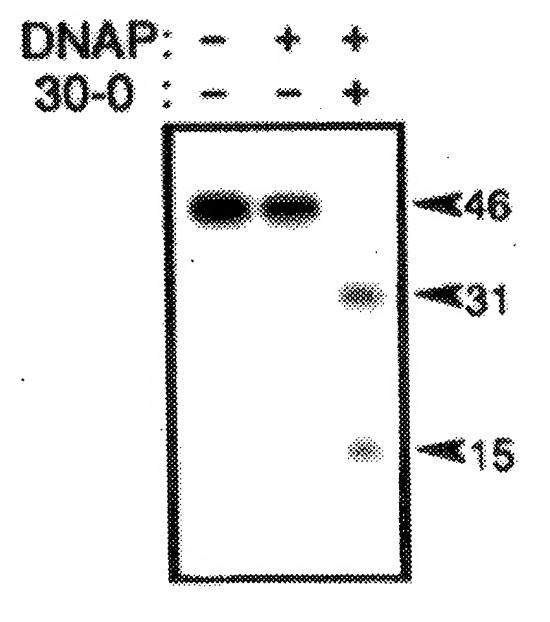


FIG. 13B



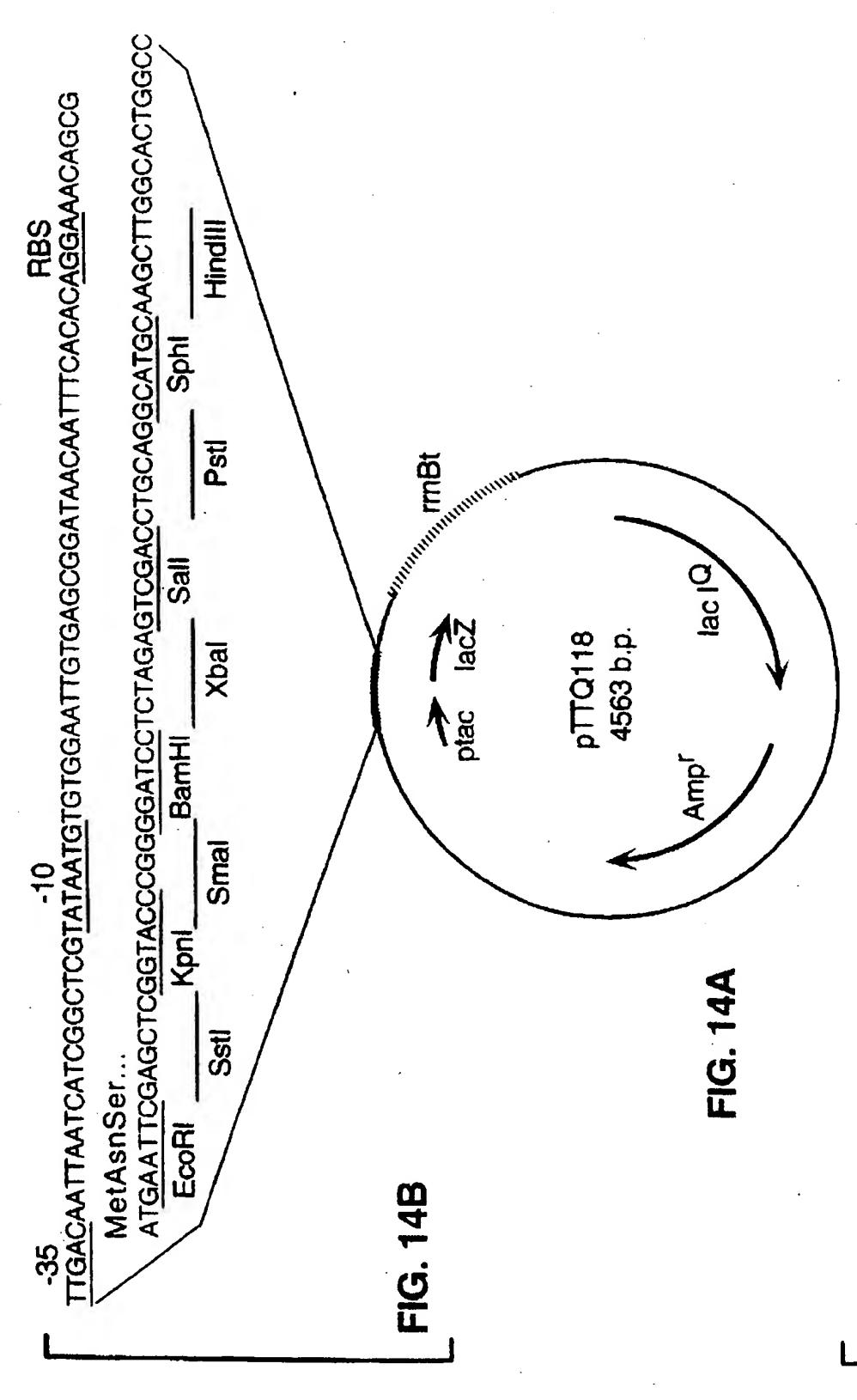
15 nt

Substrate RNA (46 nt)

AAGCUUGCAUGCCUGCAGGUCGACUCUAGAGGAUCCCC 3'
3' CGTACGGACGTCCAGCTGAGATCTCCTAGG 5'

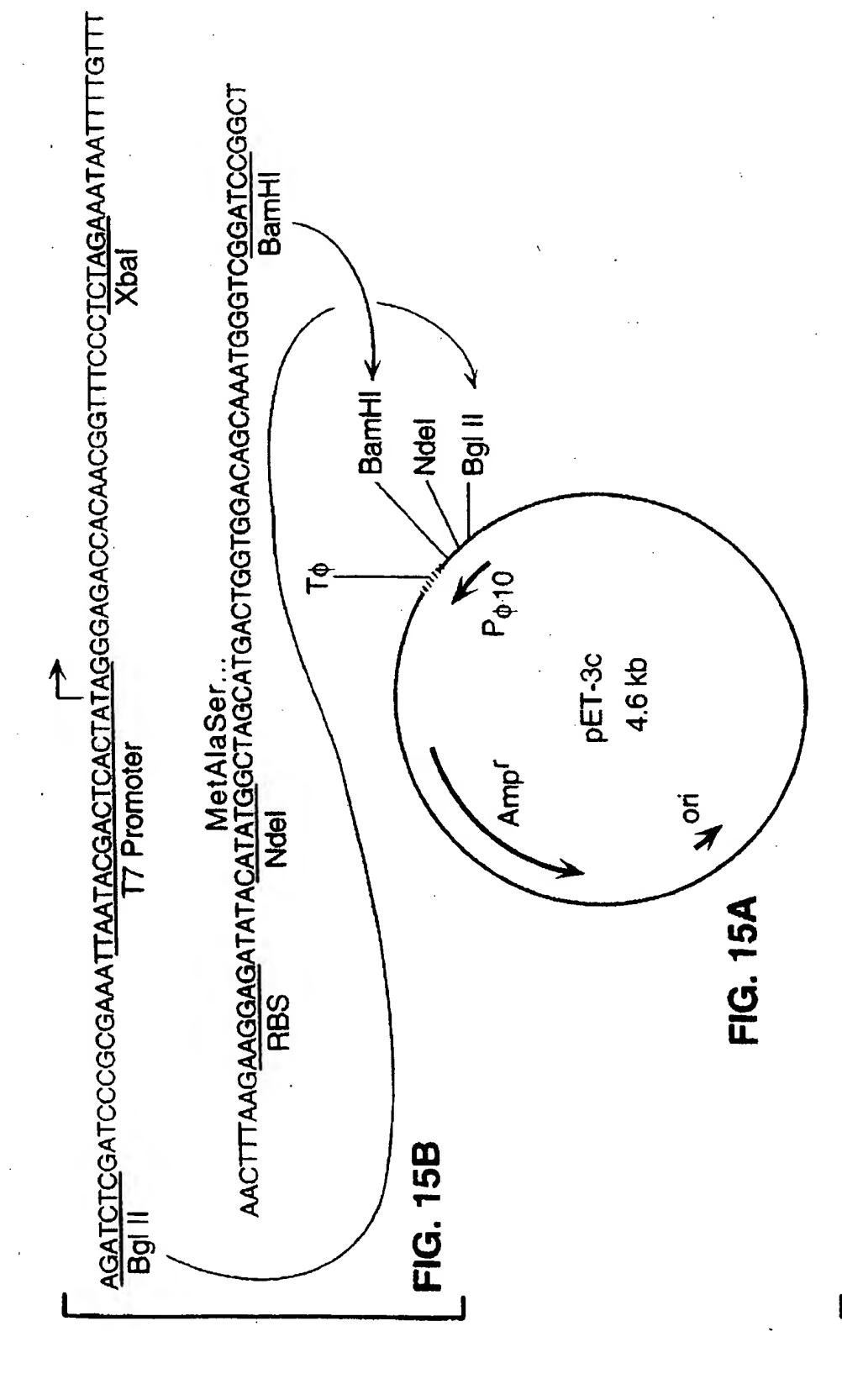
30-0

**FIG. 13A** 



rmBt: E. coli rmB transcription terminator Beta-galactosidase alpha fragment lacZ: ptac: Synthetic tac promoter RBS: Ribosome binding site lac 10: Lac repressor gene

FIG. 14C



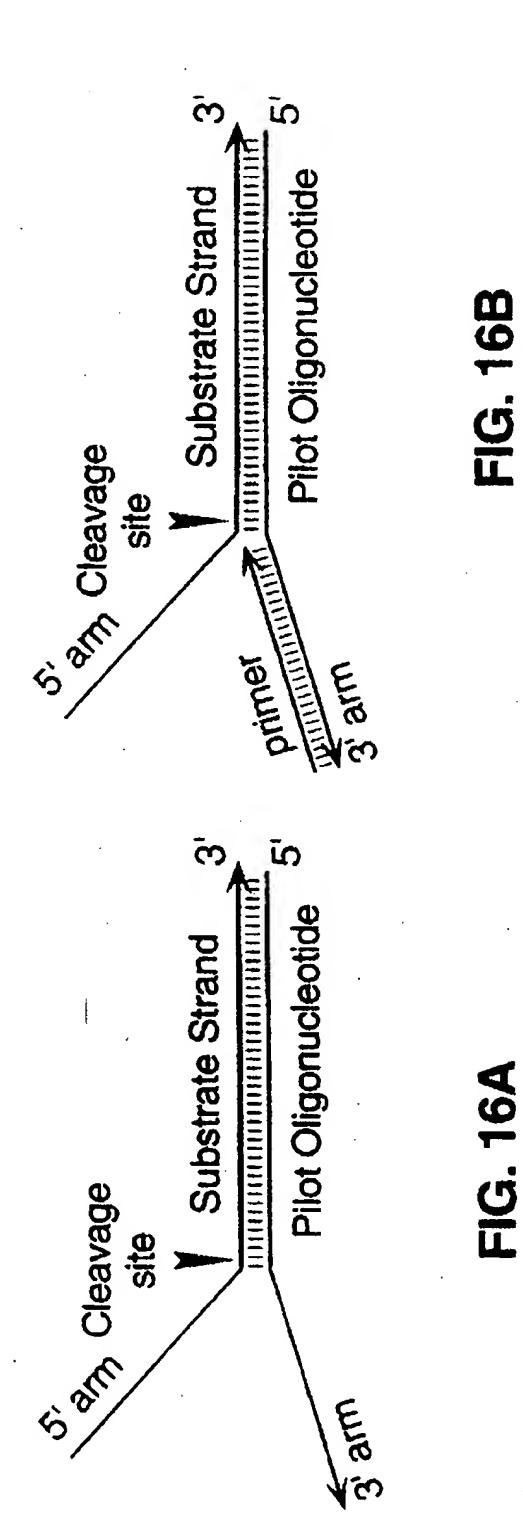
P<sub>\$10</sub>: Bacteriophage T7 \$10 promoter

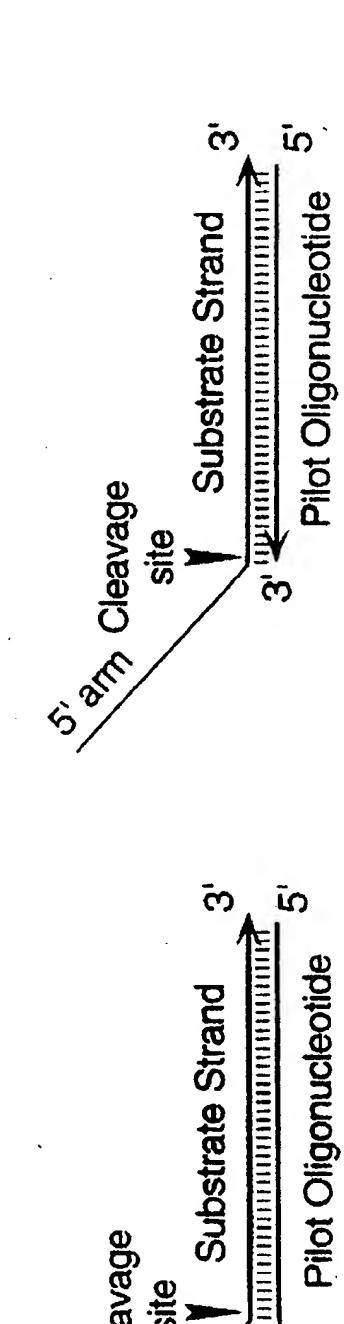
T¢: T7 ¢ Terminator

FIG. 15C

RBS: Ribosome binding site







Sy Cleavage

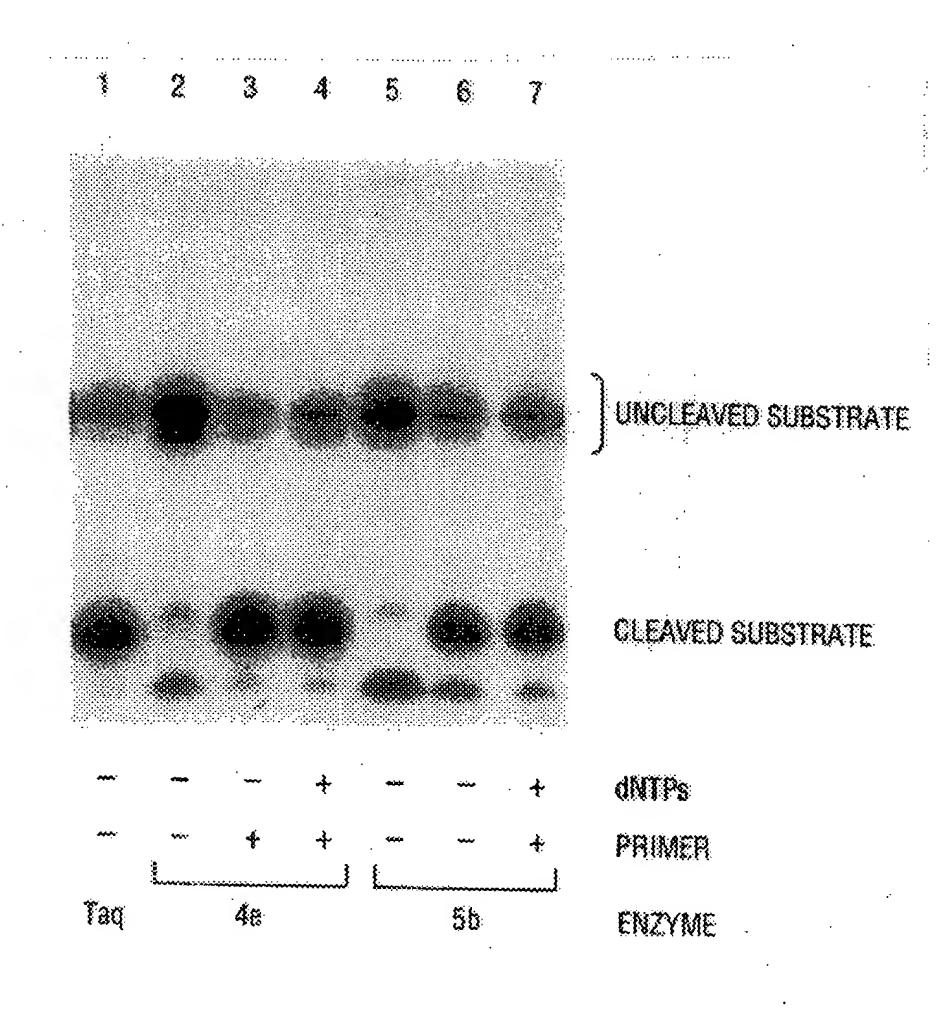
site

FIG. 16C

FIG. 16D

GCCTTAAGCTCGAGCG GG Cleavage a Sites THE SHAPE OF THE S S REAL PROCESSOR OF THE PROCESSOR OF THE

FIG. 17





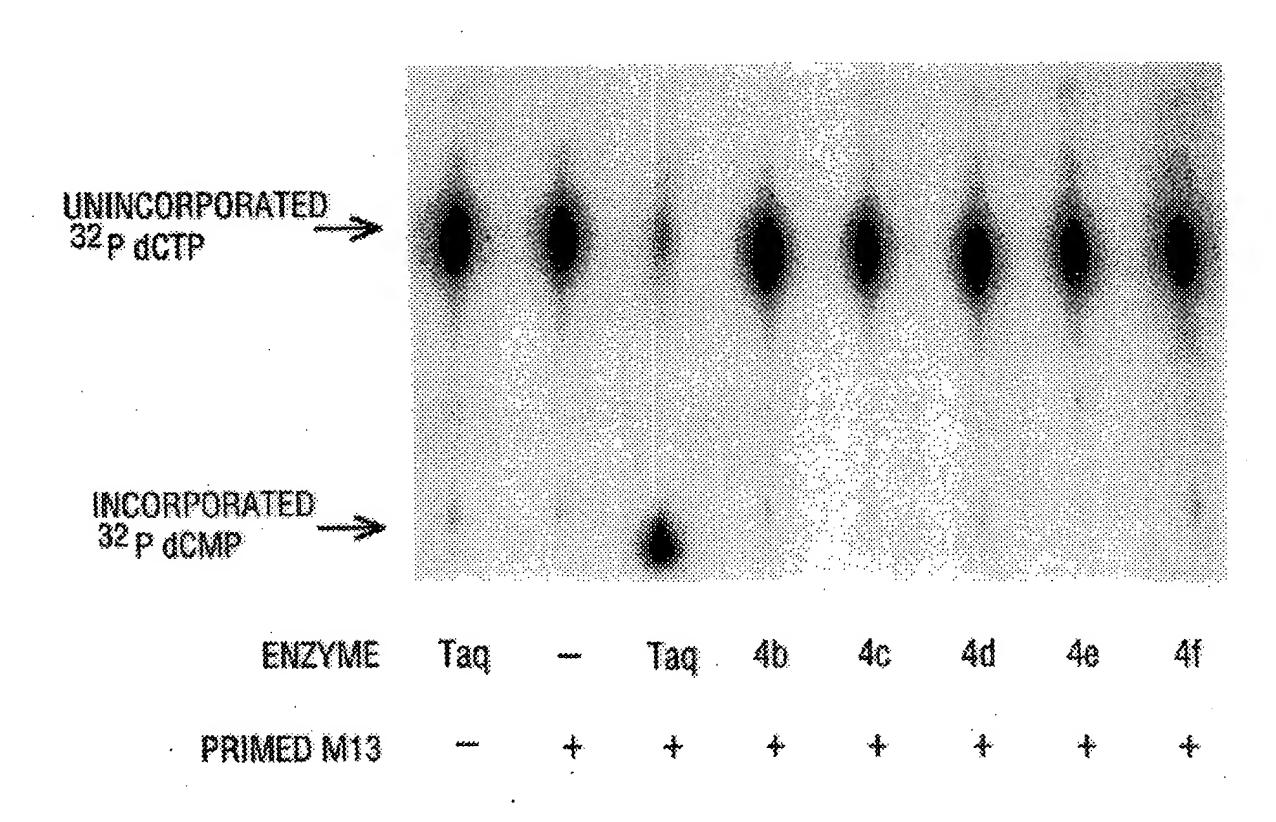


FIG. 18



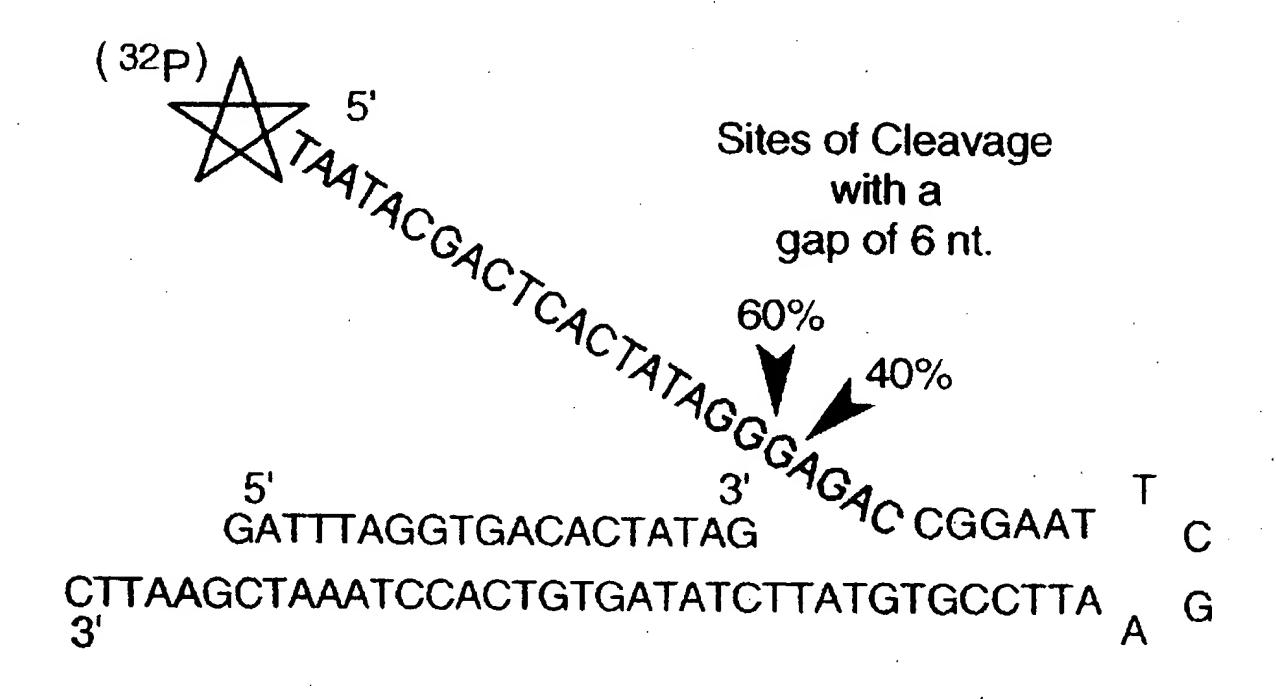
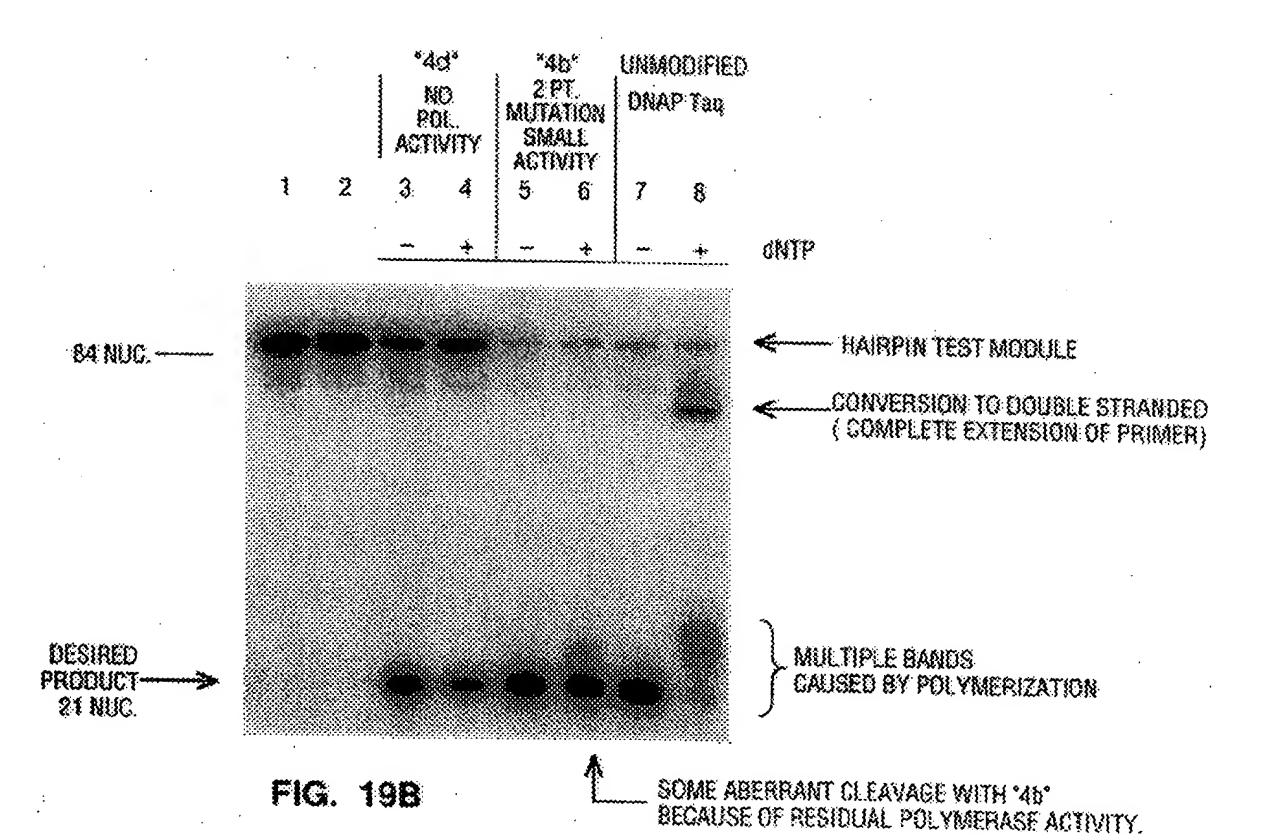


FIG. 19A







Predicted cleavage site	5' GTITCTGCTGTGTCGTCTCTTGCCTCTT	5' Alpha primer 3' CATGG + G 3' CTGCTTGTTCGCTGTGTC
T-Hairpin		
Predicted cleavage site	ACAGCGACACAG	GAGAACGGAGAA
- A-Hairpin	5' CGGACGAACAAGCGAGACAGCGACAG	5' Tau primer 3' 3' CAAAGACGACACAGCAGAGAA

FIG. 20A

Sequence of alpha primer: 5' GACGAACAAGCGAGACAAGCGAACAAGCGAGACAAGCGAGACAGCG 3'

FIG. 20B

5' CCTCTT ATACC	5' Alpha primer 3' CATGG T	3' CTGCTTGTTCGCTCTGTGTC	Cleaved T-Hairpin
CAG ATACC A C	CATGG T A	GAA	Hairpin
5' ACACAG	بري ري	AGCAGAGAGAGGAGAA	Cleaved A-Hairpin
	Tau primer	3' CAAAGACGACACAGCA	. 20C
L	ດັ	3' CAAAK	FIG.

BsmAl	Mn   Rsal	Rsal/NlalV Kpnl BsmAl
5' GTTTCTGCTGTGTCGTCTCTCTTGCC13' CAAAGACGACACAGCAGAGAGAAGGA	TCTTGTACCAT	

Ban II Sst I	Asp 718	Ava /	Kpn /	/ Xma /	Sma /	Bom HIXI
						1 YC

F Pilot 30-0 CCCCAGGGTTTTCCCCAGTCACGACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTCGAGGTCGGTACGGGGGGGATCCTC

Forward

Pst 1	BspM /	l hq2	Hind
	Sal 1	Acc /	Hinc

Reverse TAGAGTCGACCTGCAGGCATGCAAGCTTGAGTATTCTATAGTGTCACCTAAATAGCT ATCTCAGCTGGACGTCCGTACGTTCGAACTCATAAGATATCACAGTGGATTTATCGA

Pilot 30-0

	1
9	
う	1
I	+

TCCGCTCACAATTCCACACAACATACGA AGGCGAGTGTTAAGGTGTGTTGTATGCT

-48 Reverse

206



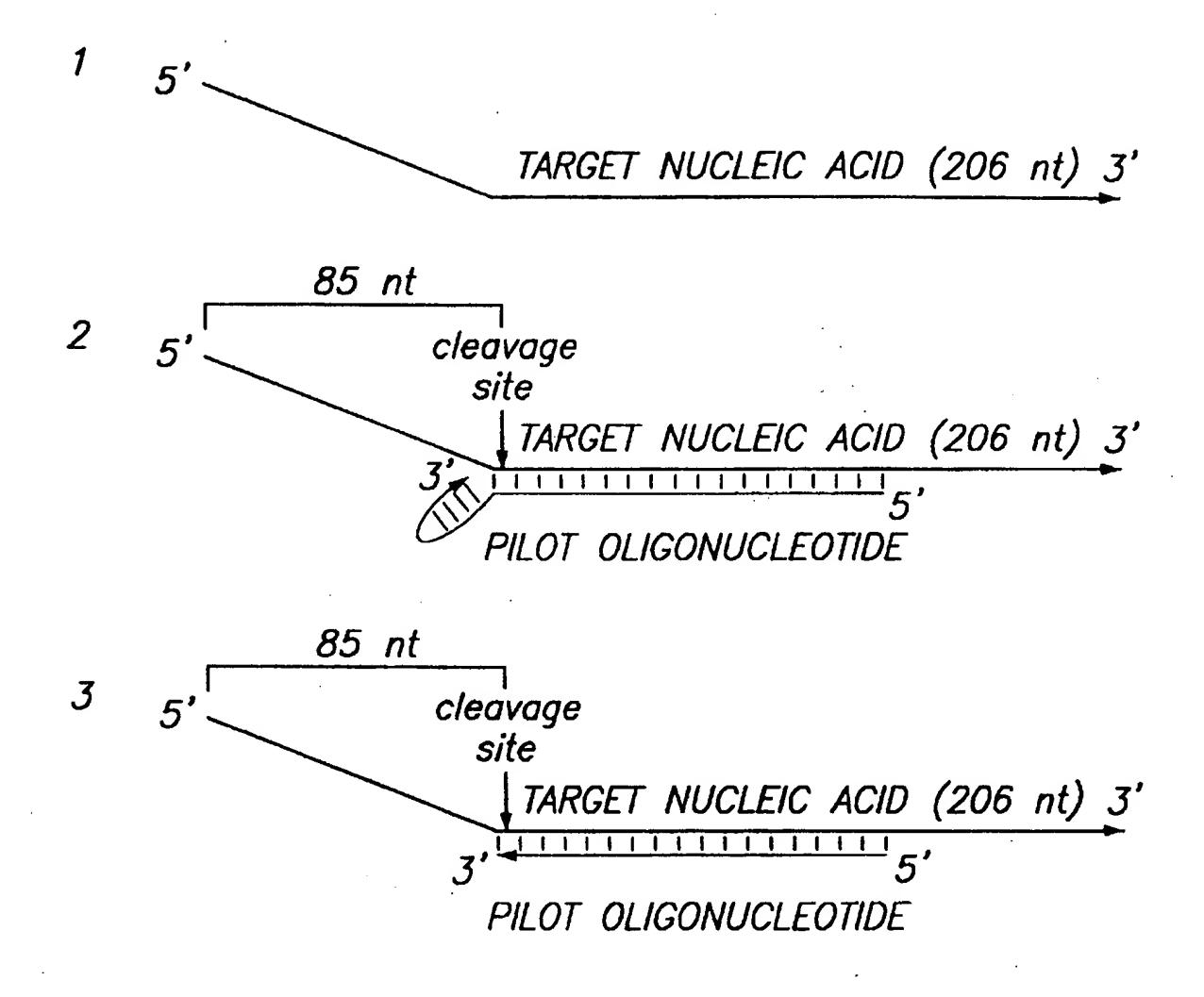


FIG. 22A



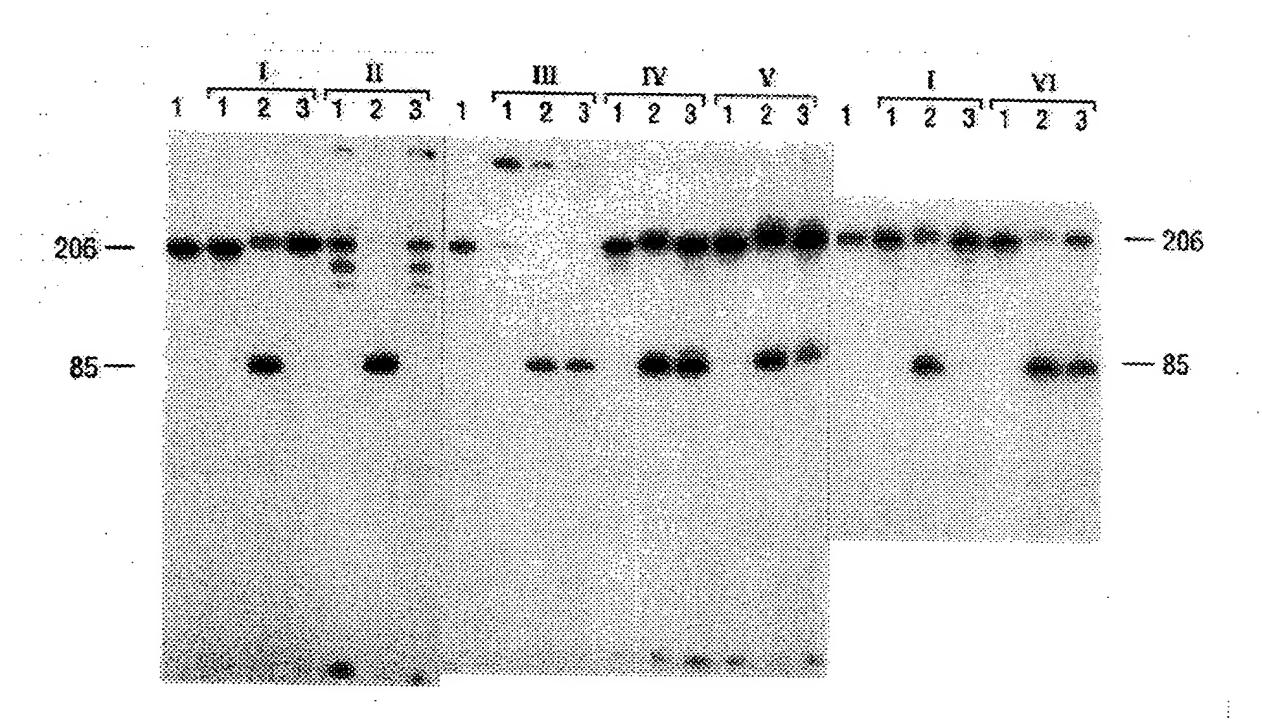


FIG. 22B

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PARADEMICAL

TRADEMICAL

TRA

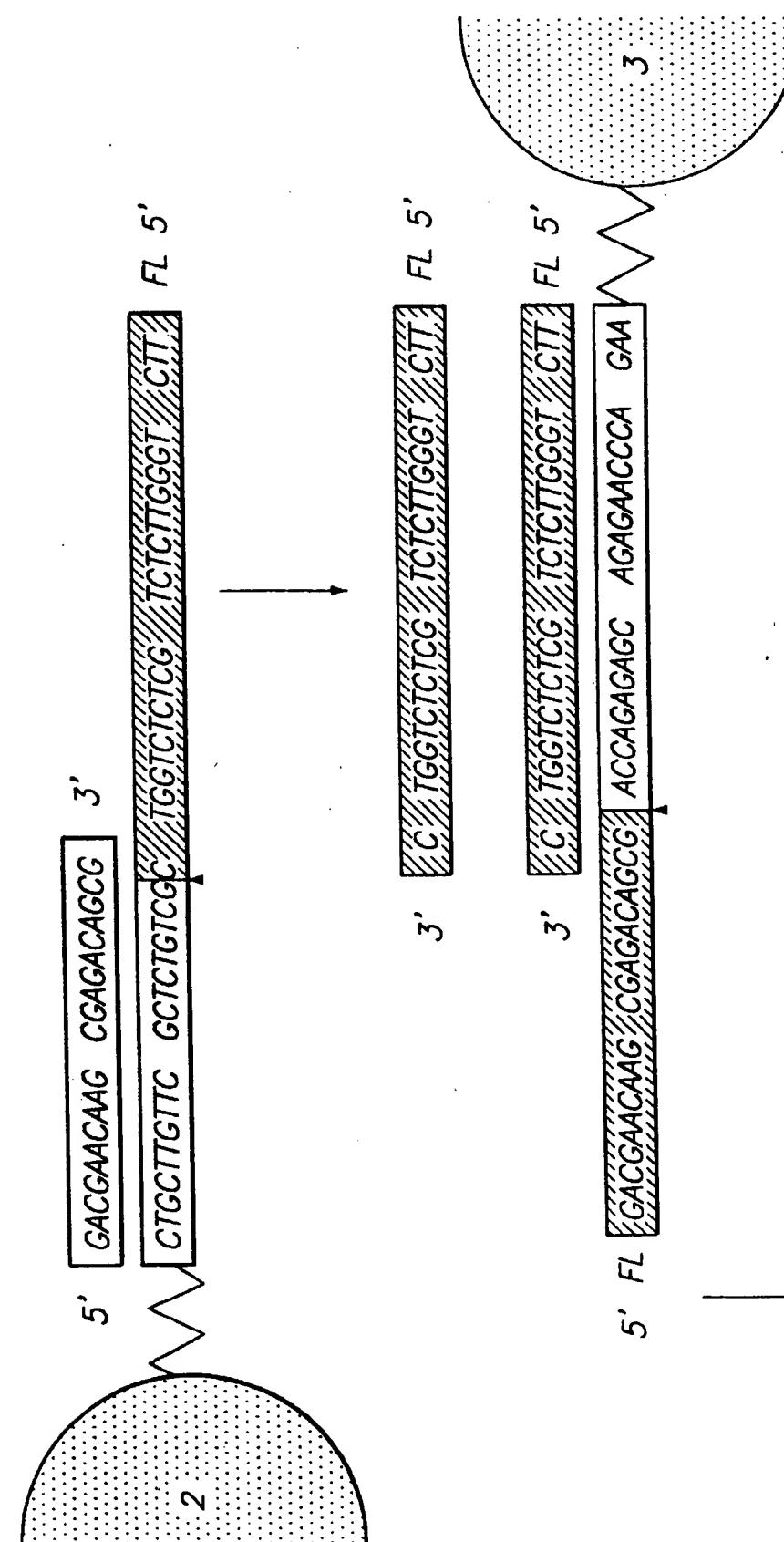


FIG. 23

5' FL & GACGAACAAG // CGAGACAGCG



COR BEAD T T T AT AT A A A
PILOT - + + + + + - - M N

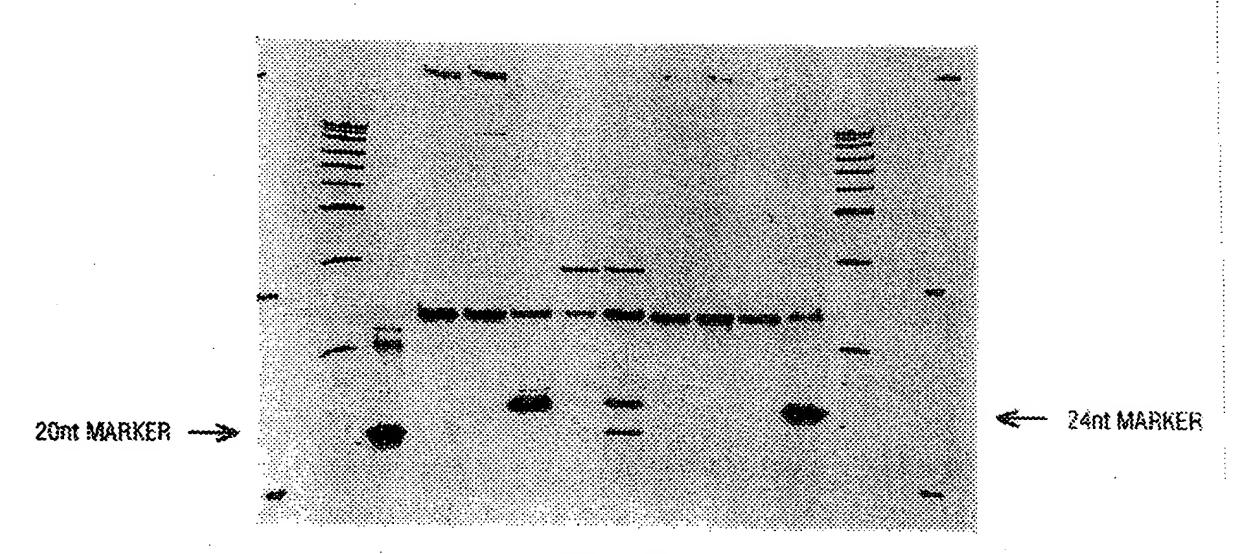


FIG. 24



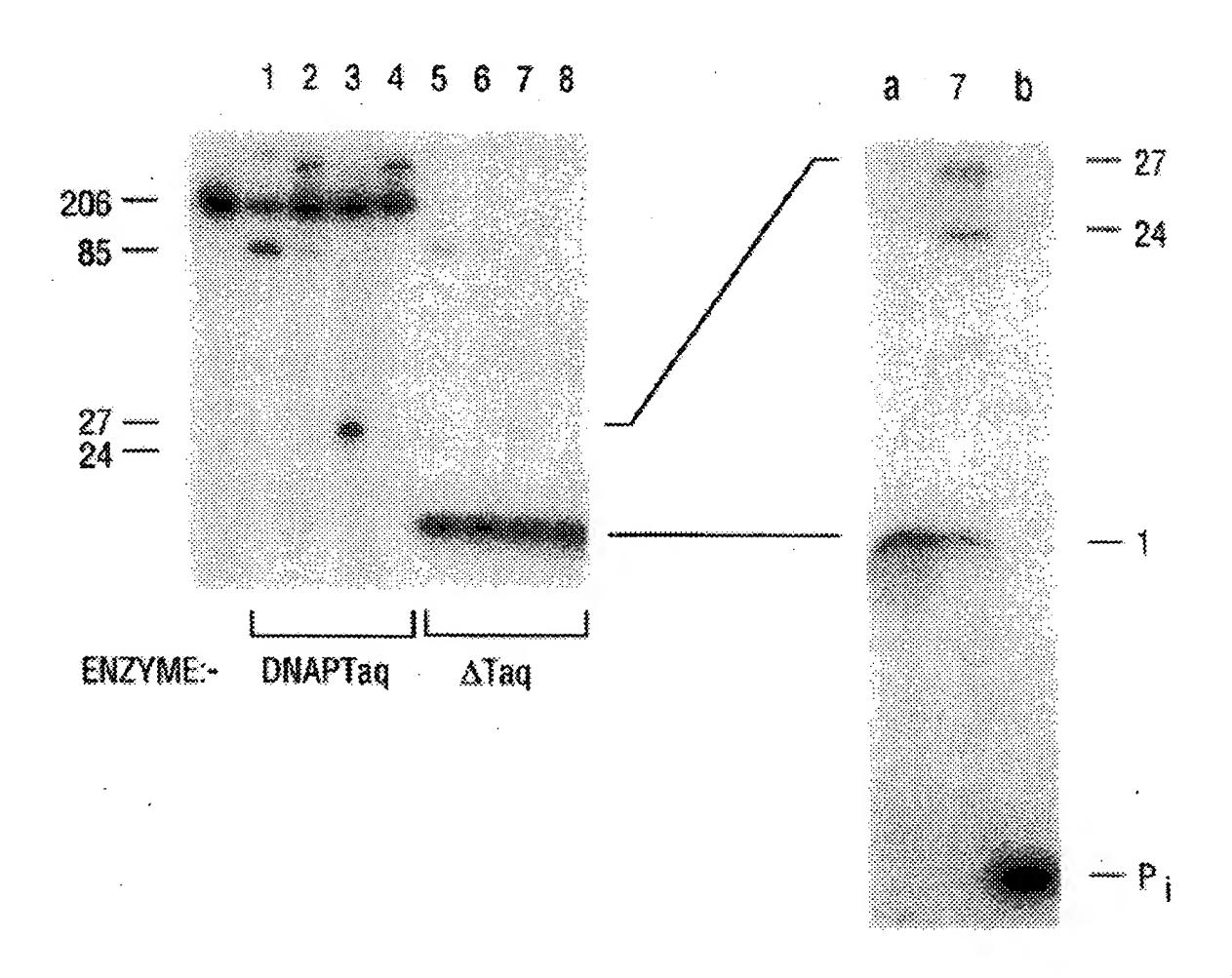
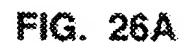


FIG. 25A

FIG. 25B





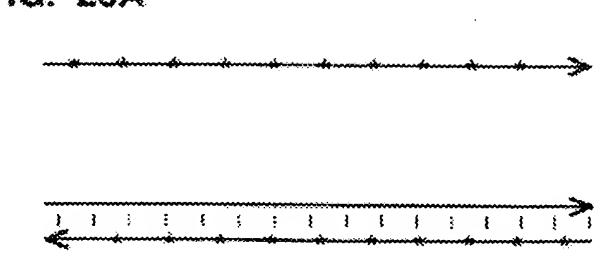
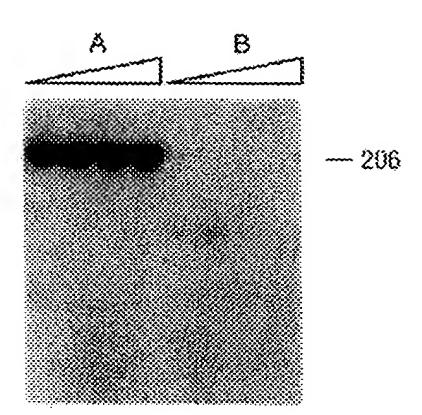


FIG. 268

\* = 32p





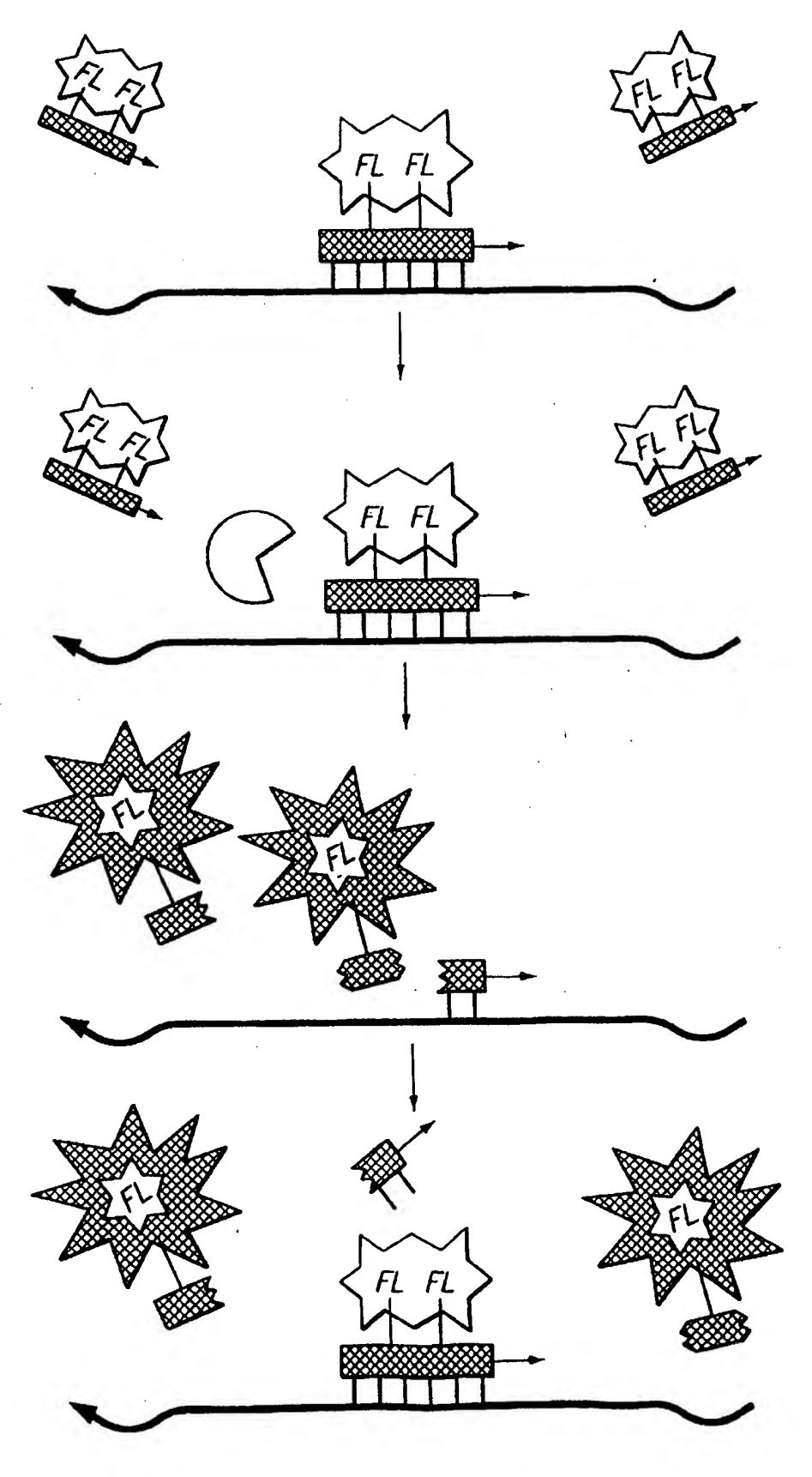


FIG. 27



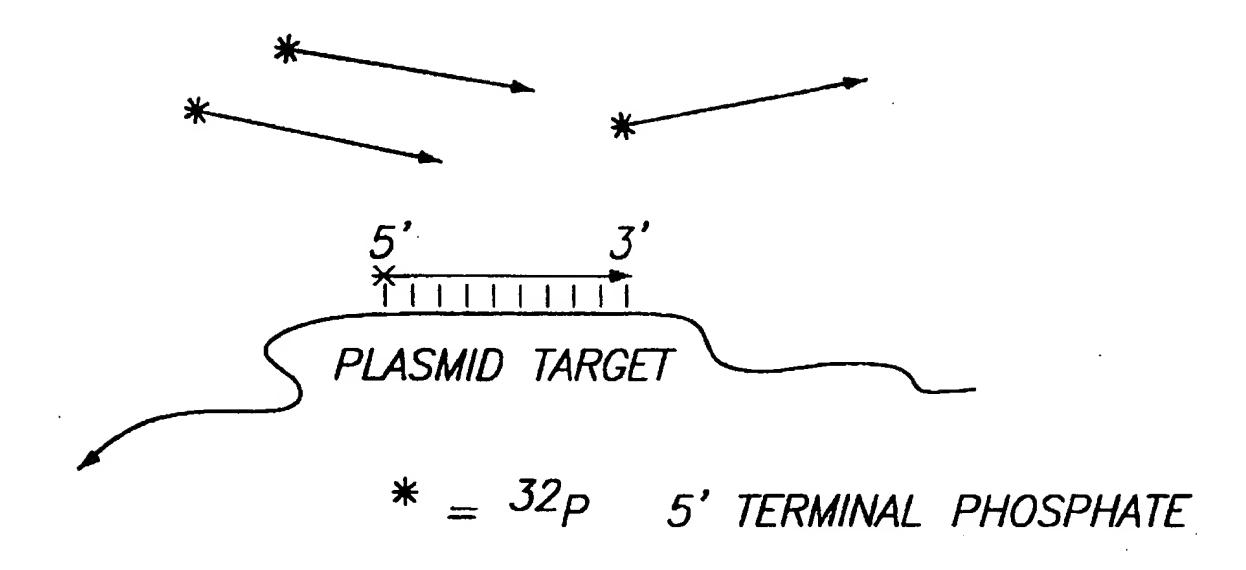


FIG. 28A



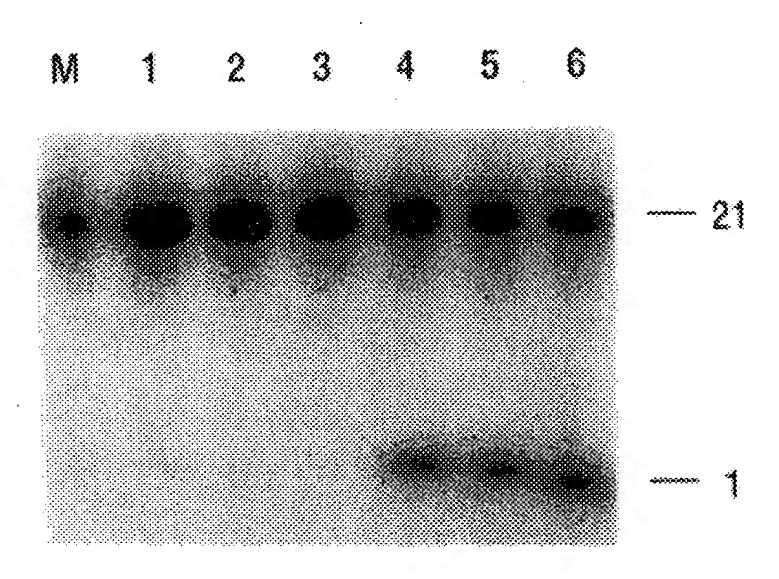


FIG. 28B



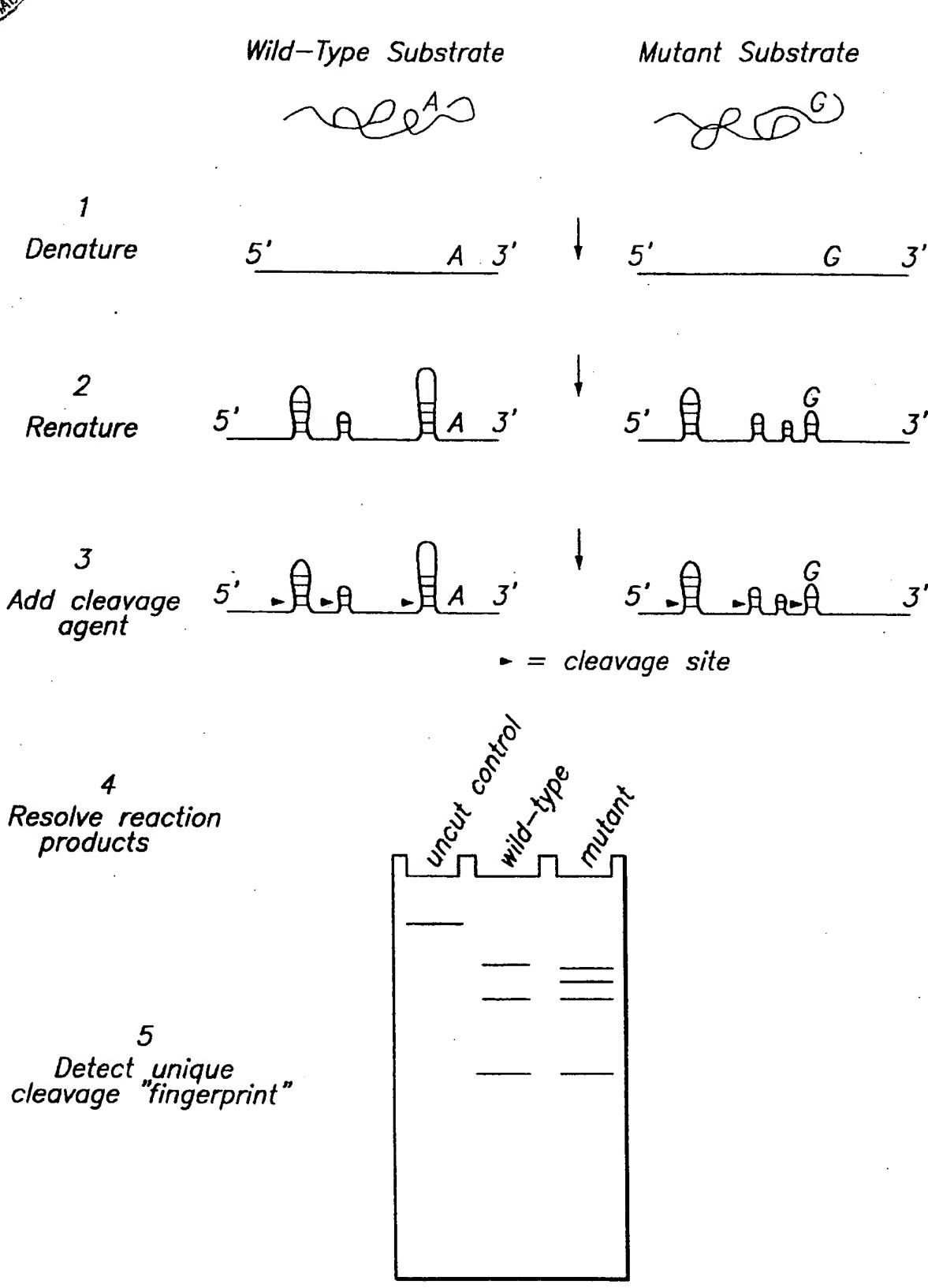


FIG. 29



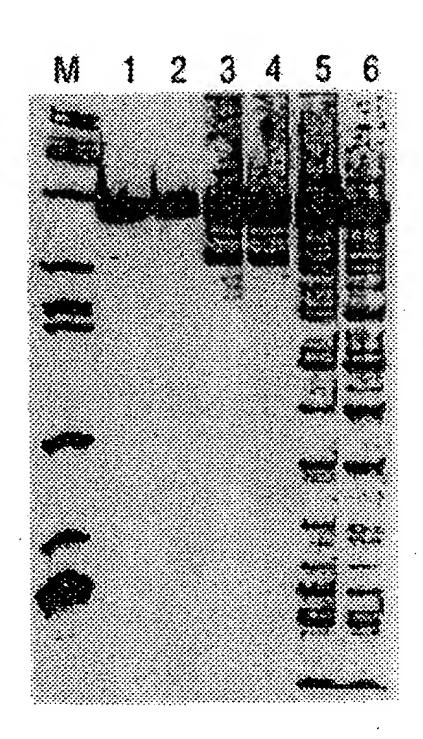


FIG. 30



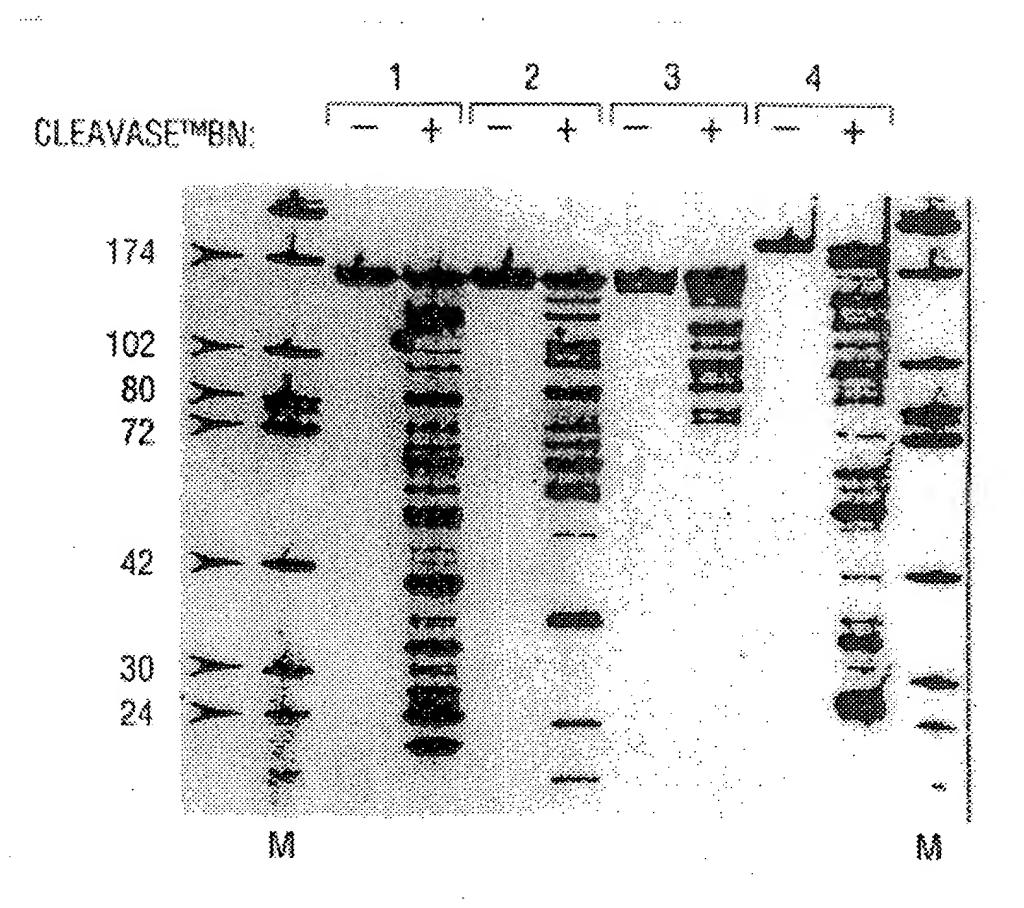


FIG. 31



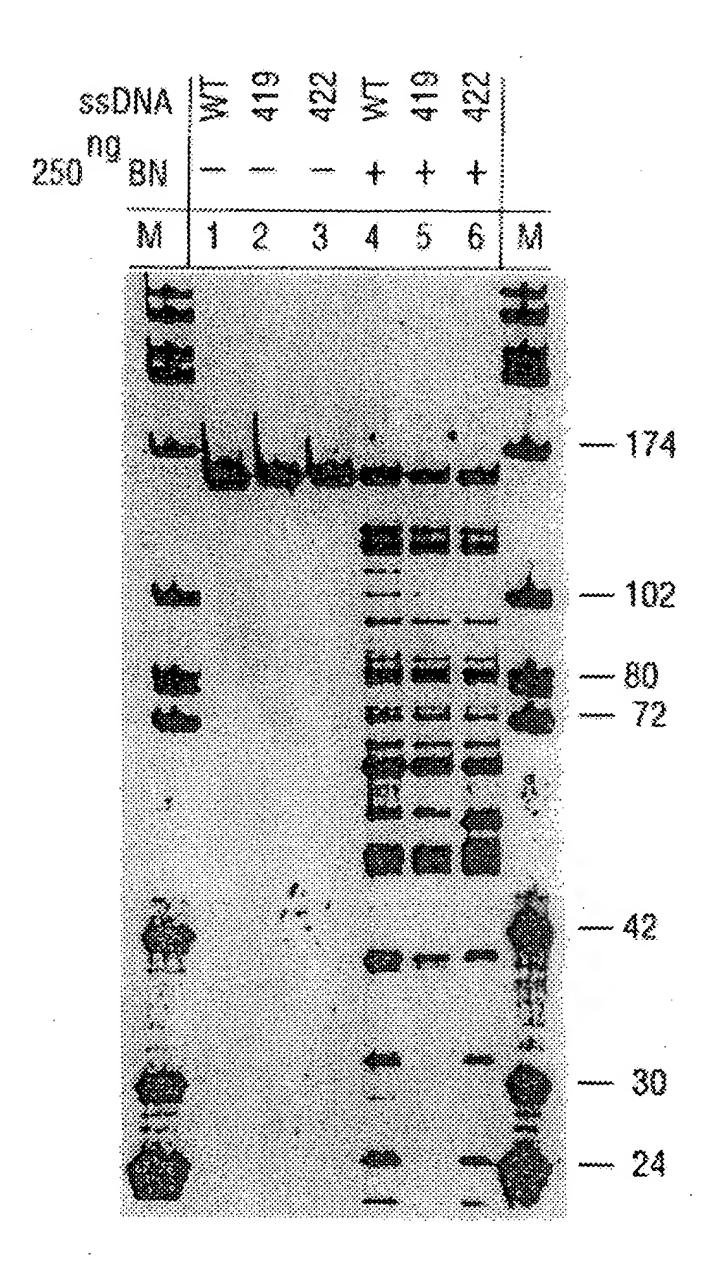


FIG. 32



157 378 1056 1587 4 1 2 3 4 5 6 7 8 M

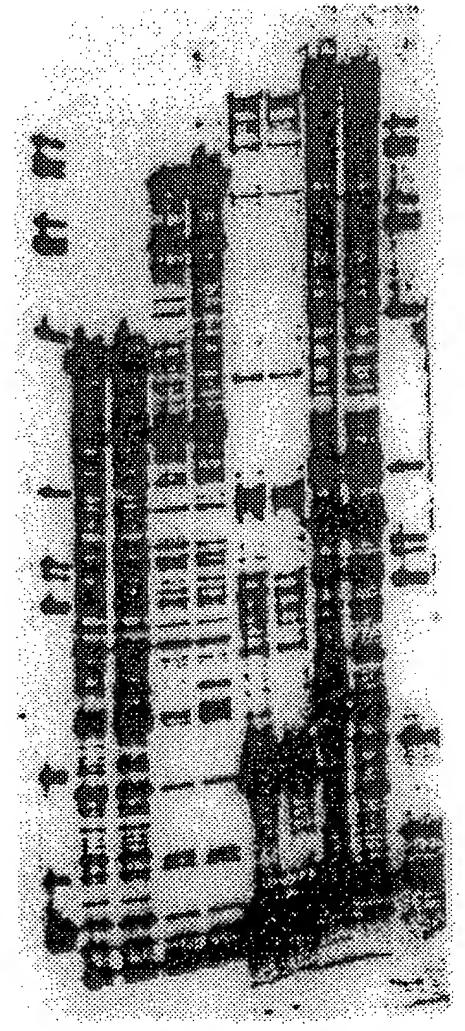


FIG. 33



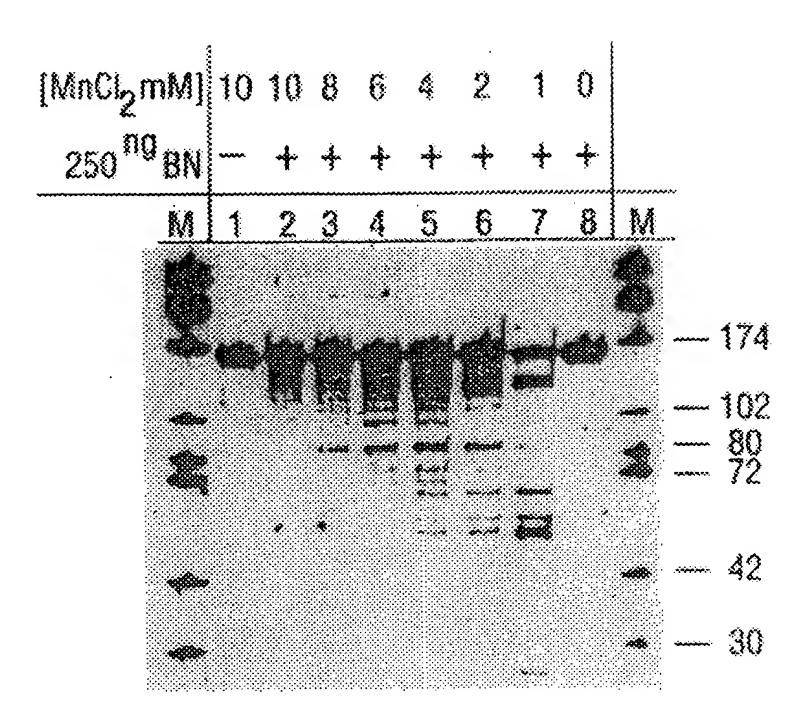


FIG. 34



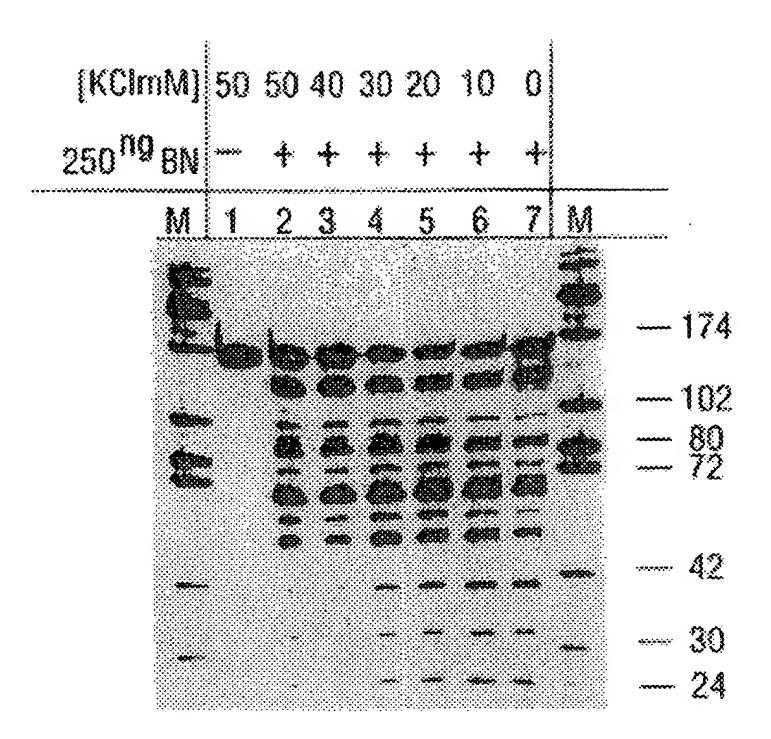


FIG. 35



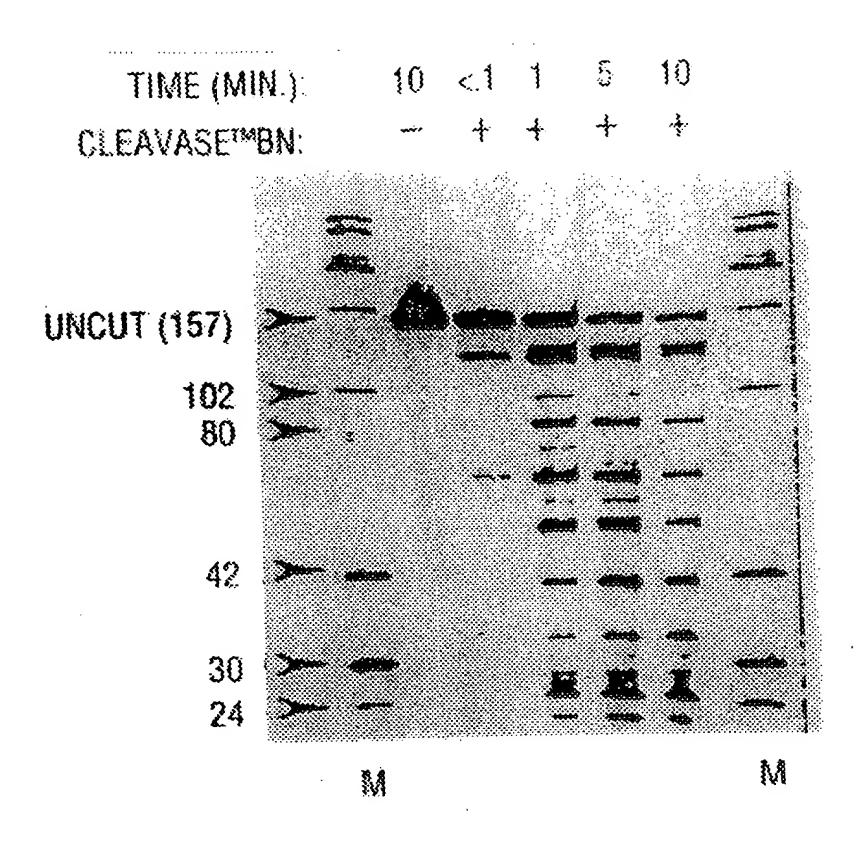


FIG. 36



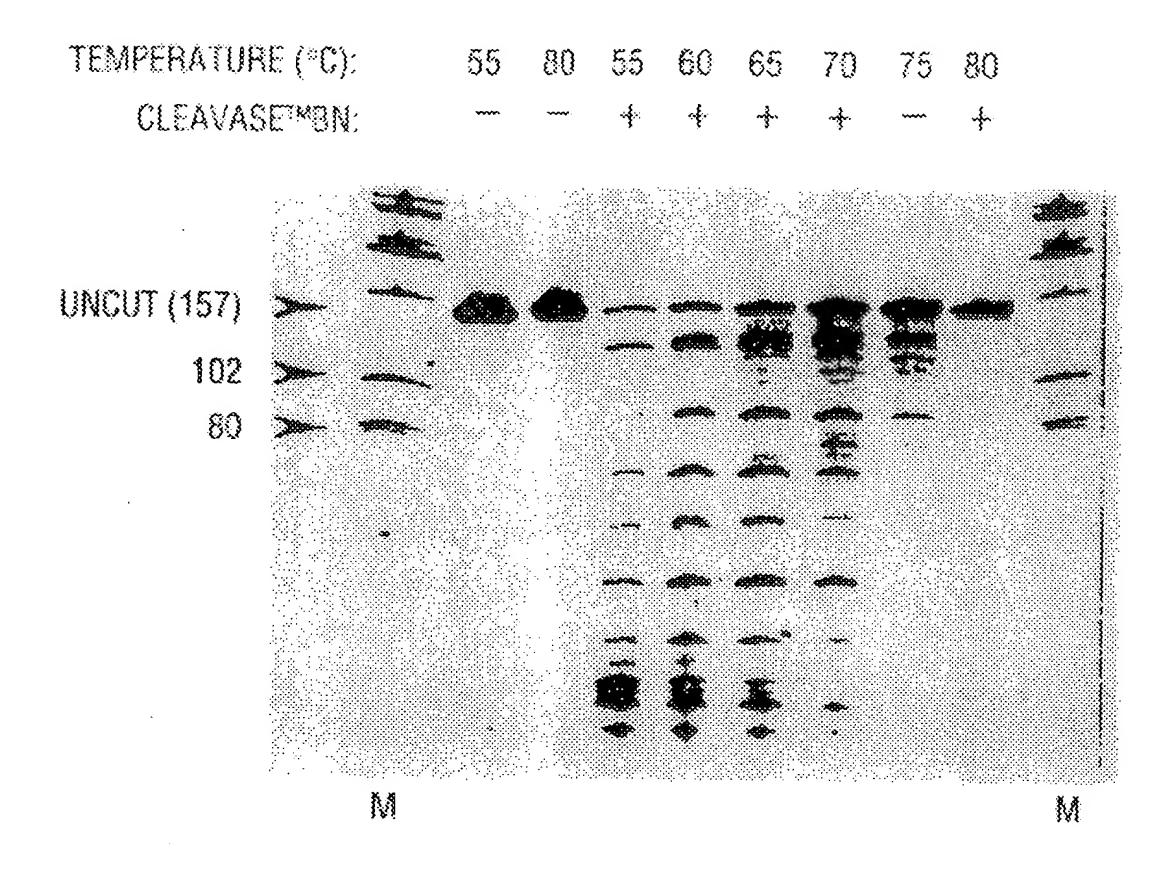


FIG. 37



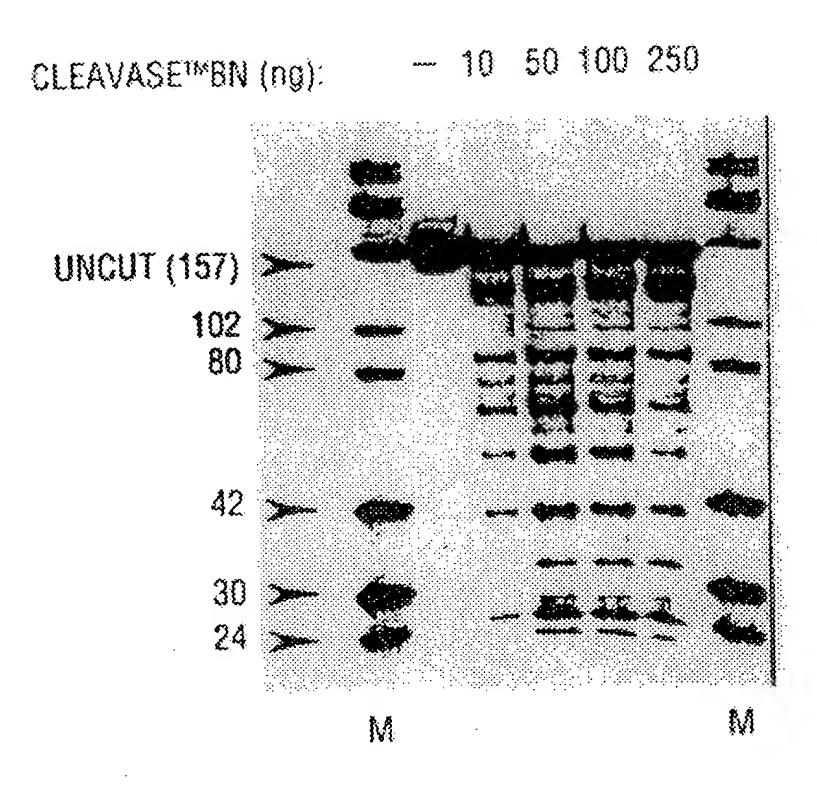


FIG. 38



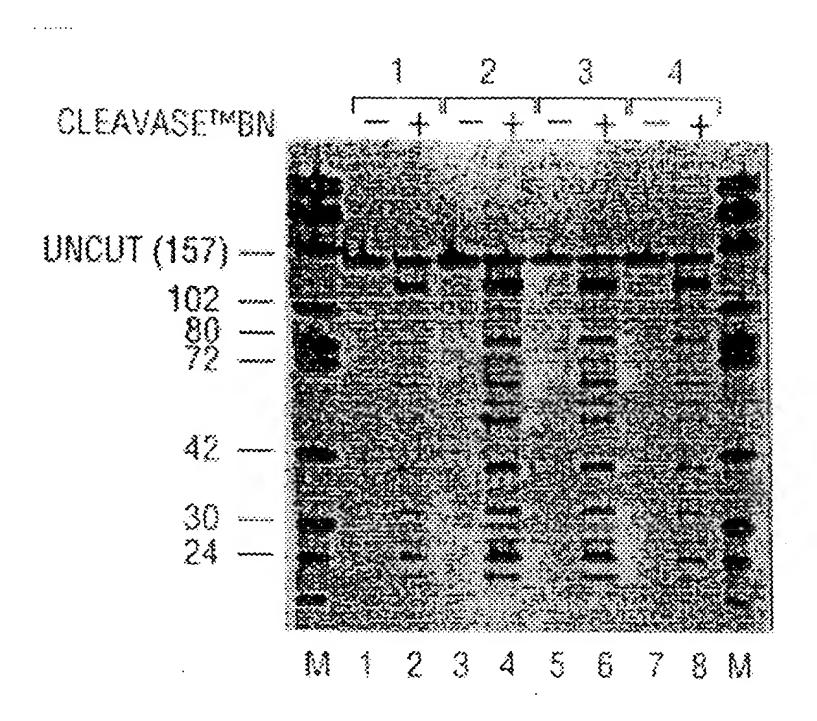


FIG. 39



ssD	NA	<b>1</b>	<b>44</b>		}	<u>2</u>			44. (2)	# <b>Q</b>		er Tr	A C C C C C C C C C C C C C C C C C C C
250 <sup>ng</sup>	BN		<b>4000</b>	<b>\$</b>	*	٠٠٠.	4.	***	4	4	••••	<b></b>	****
<u>ing nata nang papang pi</u> an	W		2	3	4	5	6	7	වි	G	10	* 1	36
												í	•
	Metacogy								<b>0.000</b>			<b>2638</b> 8	
		******	<b>X 788800</b>	<b>8</b> 0 .ee.			<b>( )</b>	<b>*</b>	, w				

FIG. 40



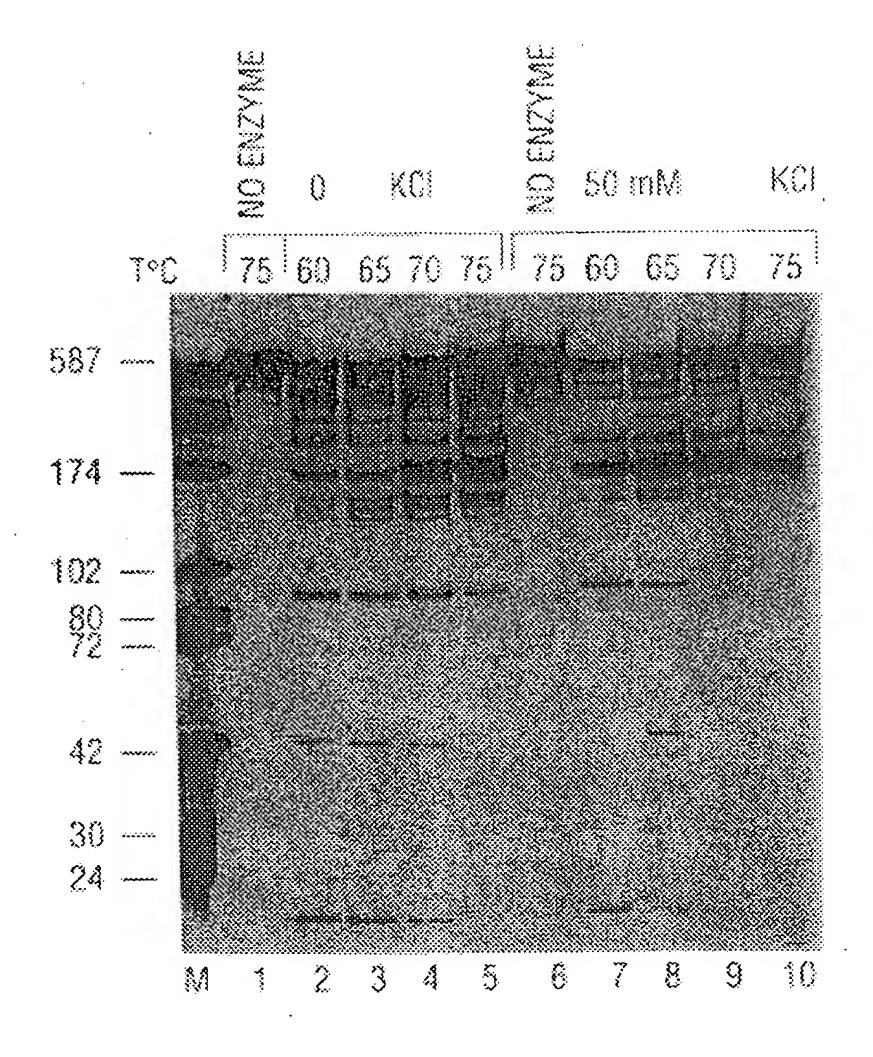


FIG. 41



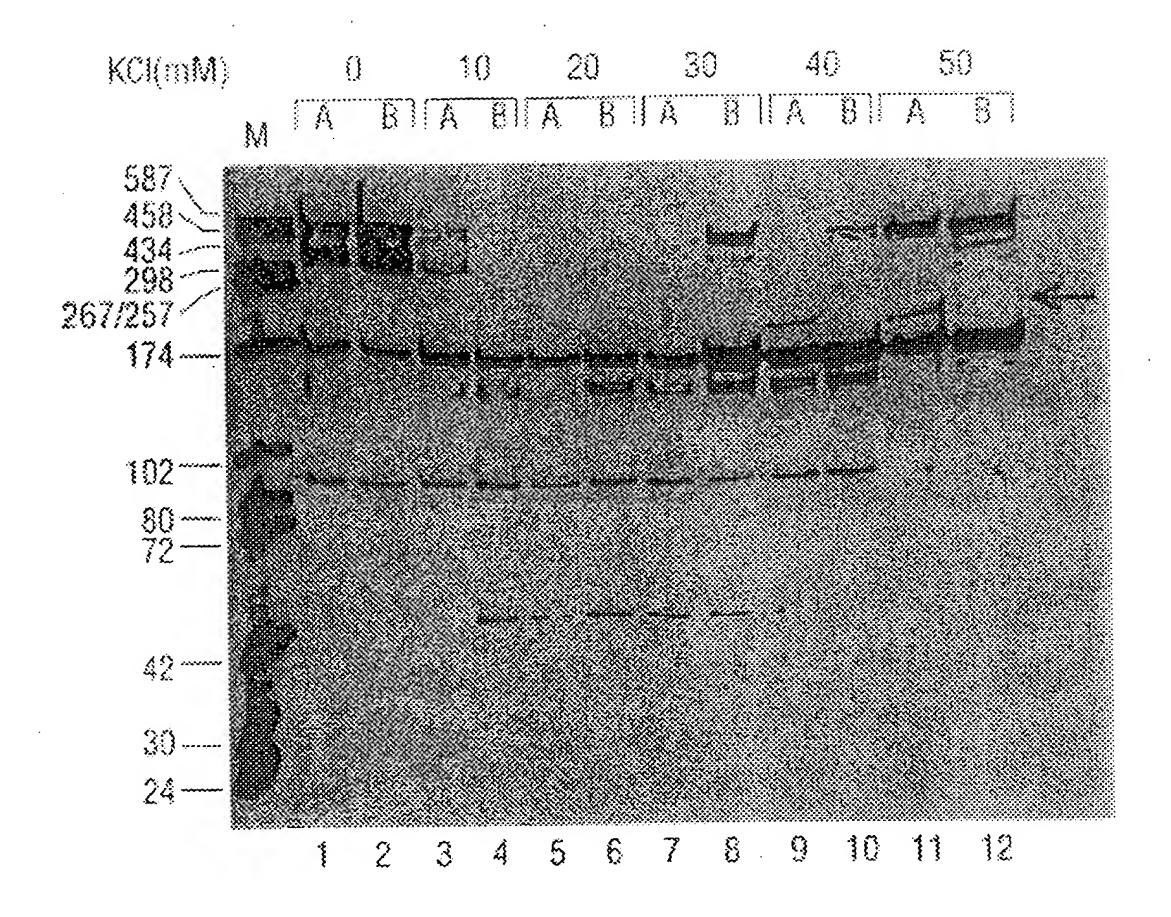


FIG. 42



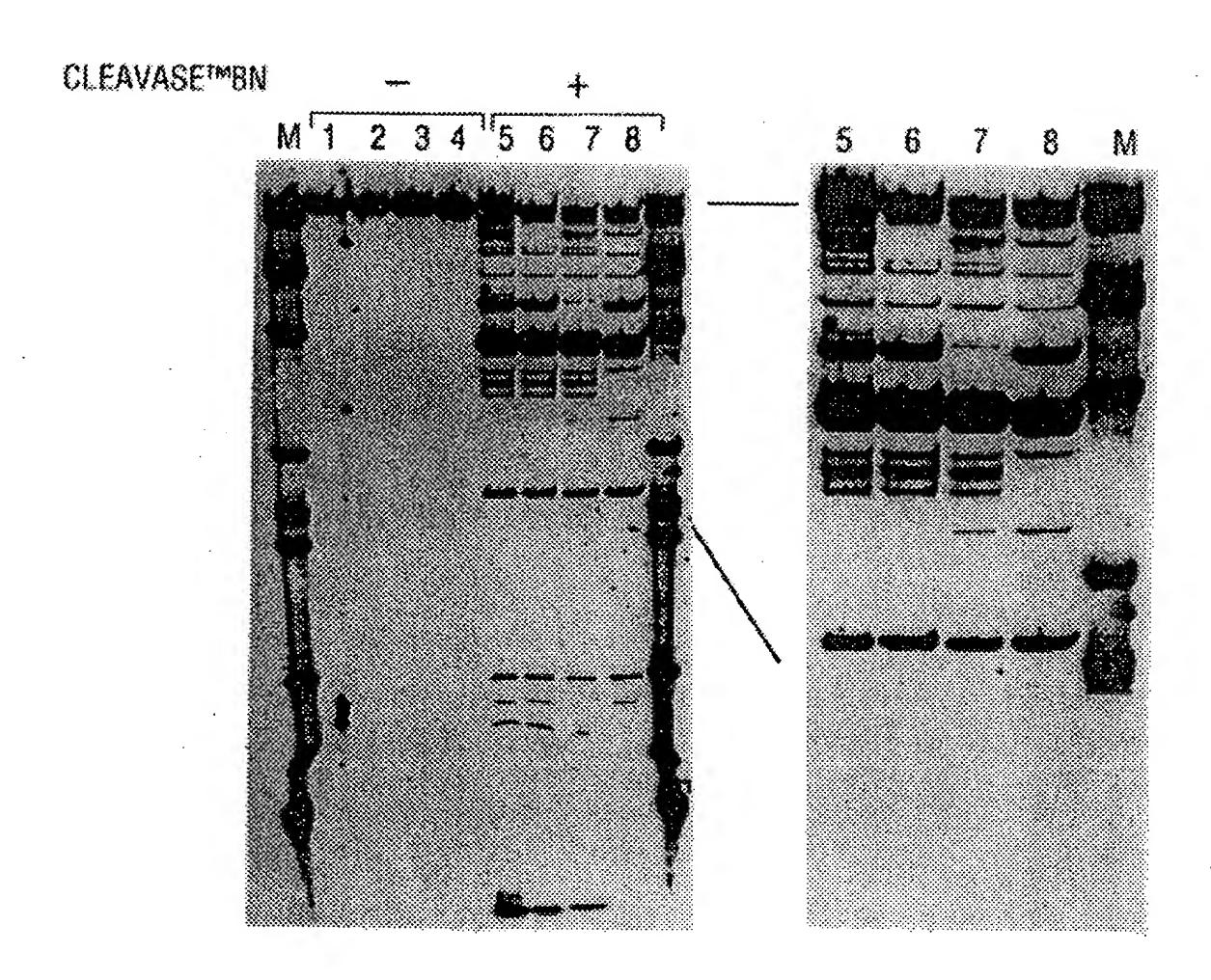


FIG. 43



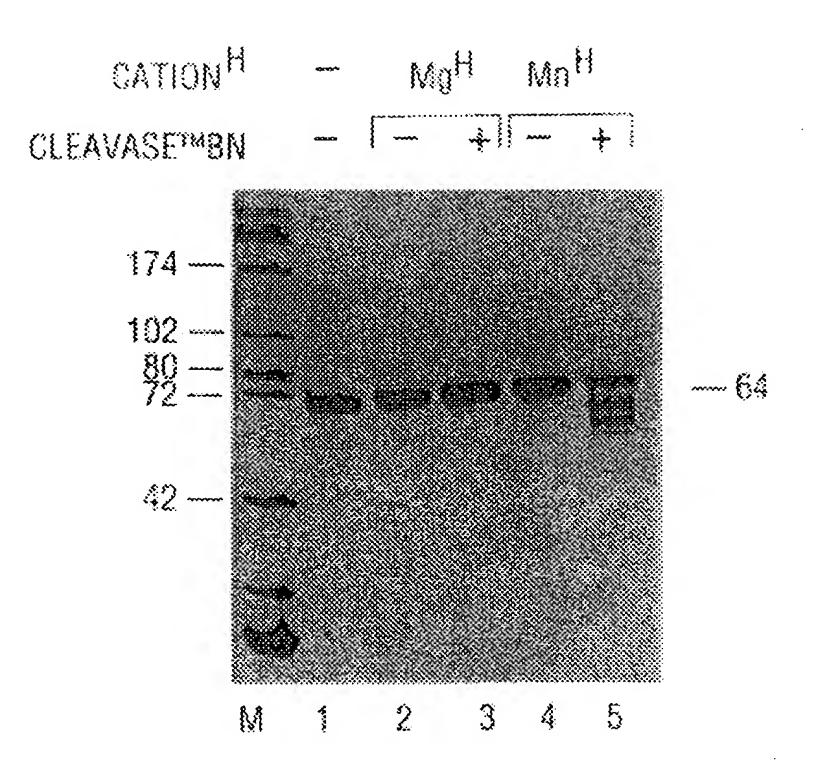
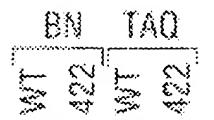
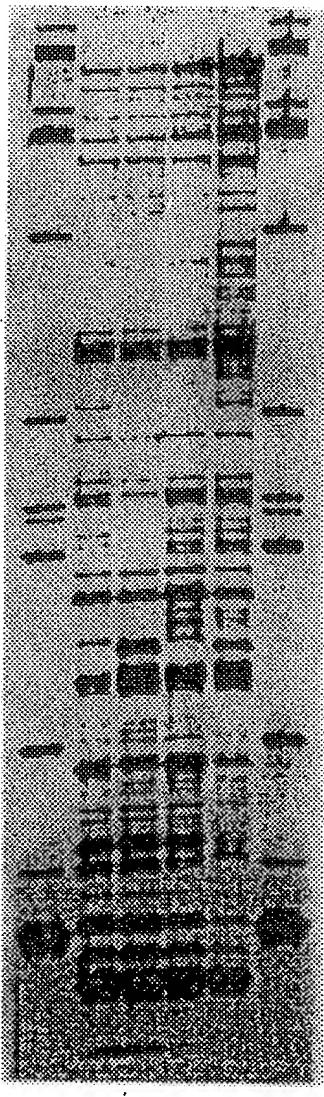


FIG. 44







M 1234 M



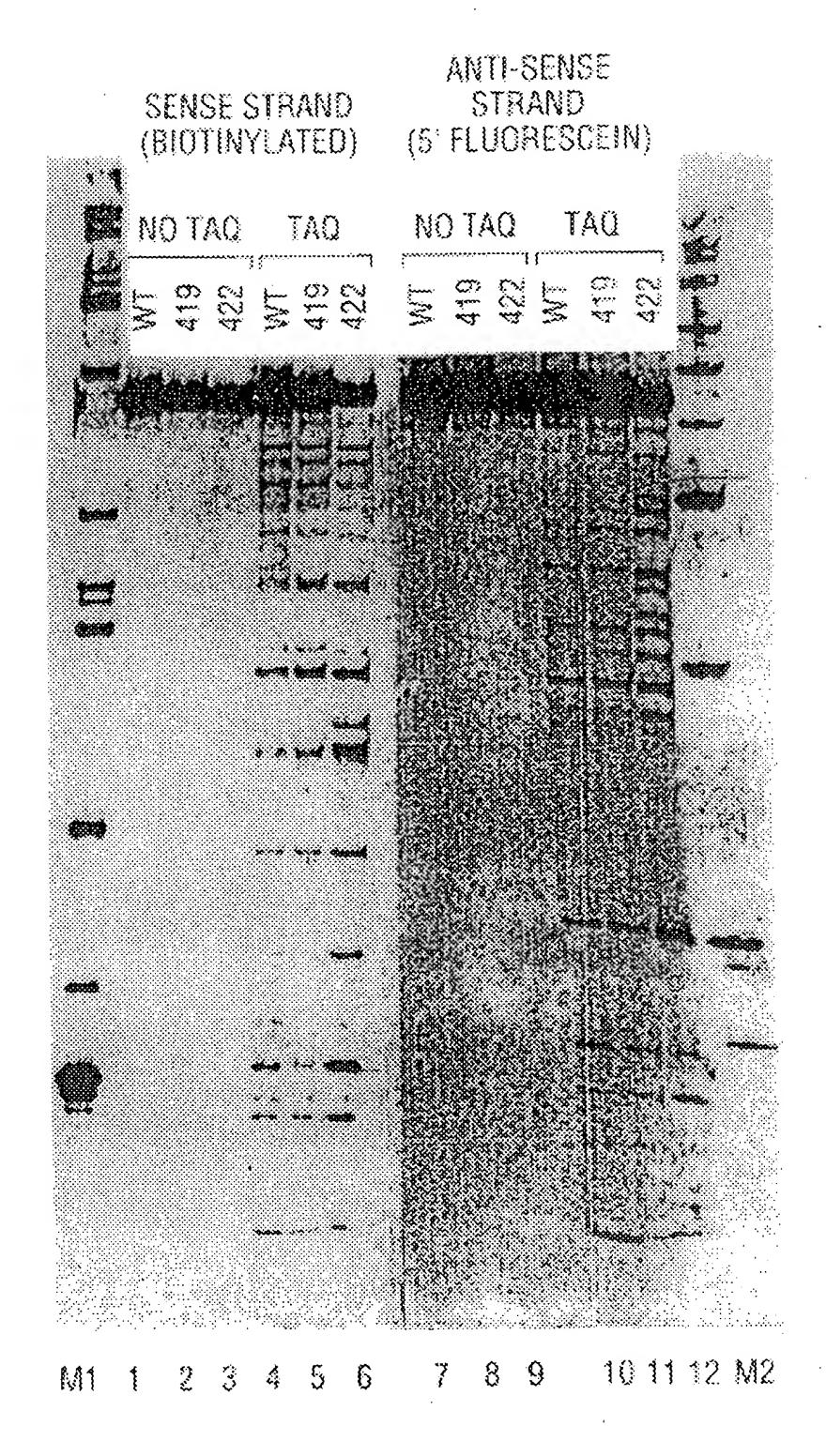


FIG. 46



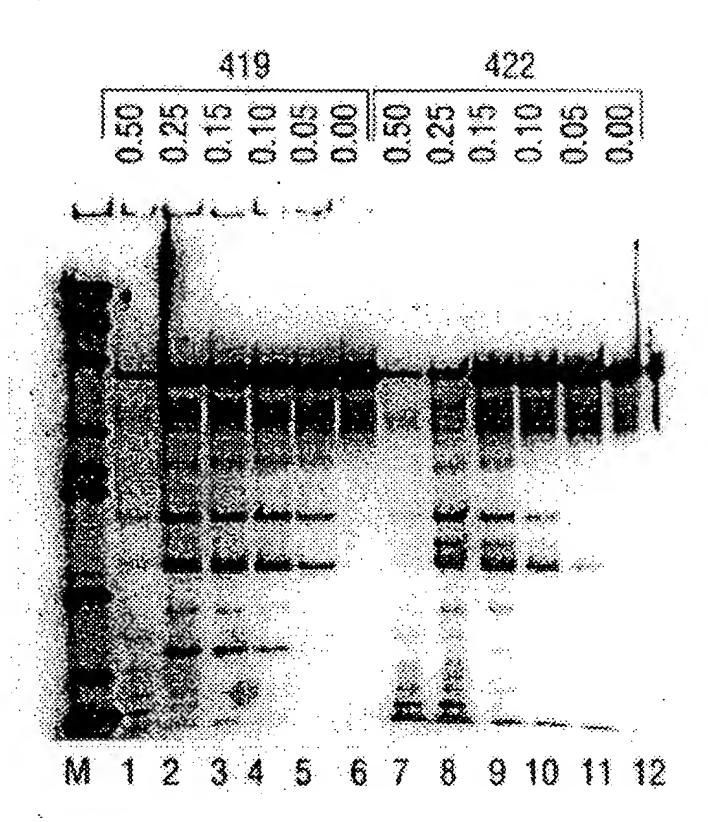


FIG. 47



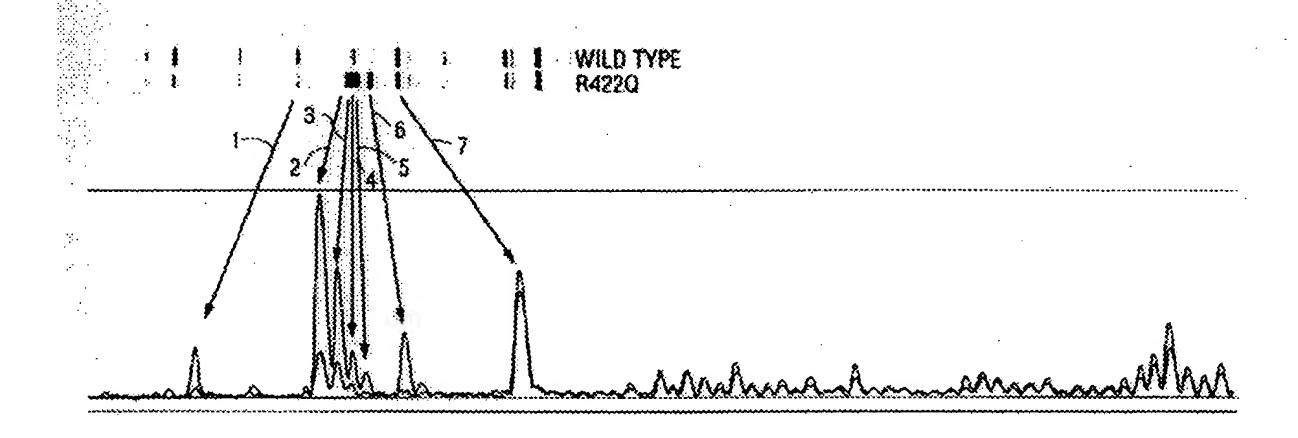


FIG. 48

GAAGGAAACTCGCTGAGACAGGGGGGCTTTCCACAAGGGGGGCCTTTCCTTTGAGGGGGGTCCTGTCCTGAAGGTGTTCCCC 5'GGCTGACAA 3'CCGACTGTT (9/ .. 0 N L.100.8-1 (SEQ ID NO 5'GGCTGACAAGAAACTCGCTGAGATAGCAGGGACTTTCCACAAGGGG 3'CCGACTGTTCTTTGAGCGACTCTATCGTCCCTGAAGGTGTTCCC 77) .. 0 N 16-10 ID L.46.

GAAGGAAACTCGCTGAGATAGCAGGGGACTTTCCACAAGGGG CTTCCTTTGAGCGACTCTTCGTCCCTGAAAGGTGTTCCCC GGCTGACAA( 7 W 78) 16-12 ID NO: L. 46. (SEQ

GAAGGAAACTCGCTGAGACAGGGGACTTTCCACAAGGGG CTTCCTTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC 5'GGCTGACAA 3'CCGACTGTT 79) .. 0 N L19.16-3 (SEQ ID <mark>ر</mark>

GAAGGAAACTCGCTGAACAGCAGGGACTTTCCACAAGGGG CTTCCTTTGAGCGACTTTGTCGTCCCTGAAAGGTGTTCCCC 5'GGCTGACAA 3'CCGACTGTT 80) CEM/251 SEQ ID NO: L. (S

GAAGGAAACTCGCTGAGACAGCAGGACTTTCCACAAGGGG CTTCCTTTGAGCGACTCTGTCGTCCTGAAAGGTGTTCCCC 5'GGCTGACAA 3'CCGACTGTT 81) . 0 N 36.8-3 EQ ID 

FIG. 49A

	1 P	200	A STATE OF THE STA	

100	ATGTTACGGGGGGGTACTGGGGGGGCCGGTCGGGAACGCCCACTCTCT	TACAATGCCCCTCCATGACCCCTCGGCCAGCCCTTGCGGGTGAGAGA
	100.8-1	(SEQ ID NO: 76)

ATGTTATGGGGAGGAGCCGGTCGGGAACACCCACTTCT TACAATACCCCTCCTCGGCCAGCCCTTGTGGGTGAAGA
L.46.16-10 (SEQ ID NO: 77)

TACAATACCCCTCCTCGGCCAGCCTTGTGGGTGAAGA	•
$ \leftarrow $	16-12 ID NO:

	<b>A</b> (
<u>ن</u>	TCGGCCAGCCCTTGCGGGGGAGAG
	999
	99
	99
ن	30
X	<u> </u>
<b>6</b> A	$C_{1}$
99	) )
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<u>9</u>	90
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9	Ù
19:	<u>ر</u>
99	0
<b>1</b> 6	AC
7	T G.
1	A
99	))
<b>GA</b>	
99	
90	<u> </u>
Ž	1
F	$\forall$
TGTI	ACA/
ATGTTACGGGGAGGTACTGGGGGGGGGCCGGTCGGGGAACGCCCCCTCTC.	TACAATGCCCCTCCATGACCCCTCC
ATGT	TACA/
ATGT	TACA/
ATGT	
ATGT	19) TACA/
ATGT	: 19)
ATGTI	: 19)
$\infty$	NO: 19)
6-3 ATGT1	: 19)
<u>~</u>	ID NO: 19)
9.16-3	ID NO: 19)
16-3	NO: 19)

ATGTTACGGGAGGTACTGGGAAGGAGCCGGTCGGGAACGCCCACTTTC	TACAATGCCCCTCCATGACCCTTCCTCGGCCAGCCCTTGCGGGTGAAAG
L.CEM/251	(SEQ ID NO: 80)

TTACGGAGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCCACTCT(	TACAATGCCTCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGTGAGAGA
3	ID NO: 81) TA(

L.36. (SEQ

L.100.8-1	150 5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGA 3'ACTACATATTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT
L.46.16-10	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGAA
L.46.16-12	5'TGGTGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGGGA 3'ACCACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCT
L.19.16-3	5'TGATGTATAAATACACTGCATTTCGCTCTGTATTCAGTCGCTCTGGGA 3'ACTACATATTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT
L.CEM/251	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACTACATATTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT
L.36.8-3	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGGGA 3'ACTACATATTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT





## FIG. 49D

 $\infty$ 

 $\infty$ 

36



250 5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG 3'TCGGACCCACAAGGGACCATCTGAGAGTGGTCGTGAACCGGCCACGACCC	AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTAGCCAGTGCTGGGTCCTGGGACCAGTCTGAGAGTGGTCGTGATCGGTCACGACCC	AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCAGTGCTGGG TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGTCACGACCC	AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGGTTGGTGGTCGTGGTGGTGGTGGTG	AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG	AGCCTGAGTGTTCCCTGCTAACTCTCACCAGCACTTGGCCGGTGCTGGG TrgGACTCACAAGGGACGATTTGAGAGTGGTCGTGACCGGCCACGACCC
5'AGCCTGGGTGTTCCCTGCTAGACT 3'TCGGACCCACAAGGGACCATCTGA	5'AGCCTGGGTGTTCCCTGCTAGACT 3'TCGGACCCACAAGGGACGATCTGA	5'AGCCTGGGTGTTCCCTGCTAGACT 3'TCGGACCCACAAGGGACGATCTGA	5'AGCCTGGGTGTTCCCTGCTAGACT3'TCGGACCACAGGGACGACGATCTG	5'AGCCTGGTGTTCCCTGCTAGAC	5'AGCCTGAGTGTTCCCTGCTAAAC
(92	77)	78)	(62	80)	× ( ×
L. 100. 8 -1 (SEQ ID NO:	L. 46.16-10 (SEQ ID NO:	L. 46.16-12 (SEQ ID NO:	L. 19.16-3 (SEQ ID NO:	L. CEM/251 (SEQ ID NO:	L. 36.8-3

HAIRPIN

FIG. 49E



	300
L. 100. 8 -1	CAGAGTGGCTCCACGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
(SEQ ID NO: 76)	GTCTCAGCGAGGTGCGAACGAATTTCTGGAGAAGTTATTCGACGC
L. 46.16-10	CAGAGTGGCTCCACGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
(SEQ ID NO: 77)	GTCTCAGCGAGGAACGAACGAATTTCTGGAGAAGTTATTCGACGG
L. 46.16-12	CAGAGTGGCTCCACGCTTGCTTAAAGACCTCTTCAATAAGCTGCC
(SEQ ID NO: 78)	GTCTCAGCGAGGACGAACGAATTTCTGGAGAAGTTATTCGACGG
L. 19.16-3	CAGAGTGGCTCCACGCTTGCTTAAAGACCTCTTCAATAAGCTGCC
(SEQ ID NO: 79)	GTCTCAGCGAGGTGCGAACGAATTTCTGGAGAAGTTATTCGACGG
L. CEM/251	CAGAGTGACTCCACGCTTGCTTAAAGCCCTTTTCAATAAGCTGCC
(SEQ ID NO: 80)	GTCTCAGTGAGGAACGAATTTCGGGAGAGATTTTCGGGGGGAGAGTTATTCGACGG
L. 36.8-3	CAGAGCGGCTCCACGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
(SEQ ID NO: 81)	GTCTCGGCGAGGAACGAACGAATTTCTGGAGAAGTTATTCGACGG

FIG. 49F

HAIRPIN



	350	
L.100.8-1	5'ATTTTAGAAGTAGGCCAGTGTGTTCCCATCTCCTAGCCGCCGCCTG 3'TAAAATCTTCATCCGGTCACACACAGGGTAGAGGGATCGGCGGGGGAC	G 3°
L.46,16-10	5 'ATTTAGAAGTAAGCCAGTGTGTGTTCCCATCTCCTAGCCGCCGCCTG 3 'TAAAATCTTCATTCGGTCACACAAGGGTAGAGAGGATCGGCGGGGGAC	G 3 -
L.46.16-12	5'ATTTTAGAAGTAAGCCAGTGTGTTTCCCATCTCCTAGCCGCCGCCTG 3'TAAAATCTTCATTCGGTCACACACAGGGTAGAGGGATCGGCGGCGGAC	G 3
L.19,16-3	5'ATTTTAGAAGTAGGCTAGTGTGTTCCCATCTCCTAGCCGCCGCCTG 3'TAAAATCTTCATCCGATCACACACGGGGGTAGAGGGATCGGCGGGGGGAC	G 3 '
L.CEM/251	5'ATTTTAGAAGTAAGCTAGTGTGTTCCCATCTCCTAGCCGCCGCTG 3'TAAAATCTTCATTCGATCACACACAGGGTAGAGAGGATCGGCGGGGGAC	G 3'
L.36.8-3	5'ATTTTAGAAGTAGGCTAGTGTGTGTTCCCATCTCCTAGCCGCCGCCTG 3'TAAAATCTTCATCCGATCACACACAGGGTAGAGAGGGATCGGCGGCGGGAC	G 3'

## FIG. 49G



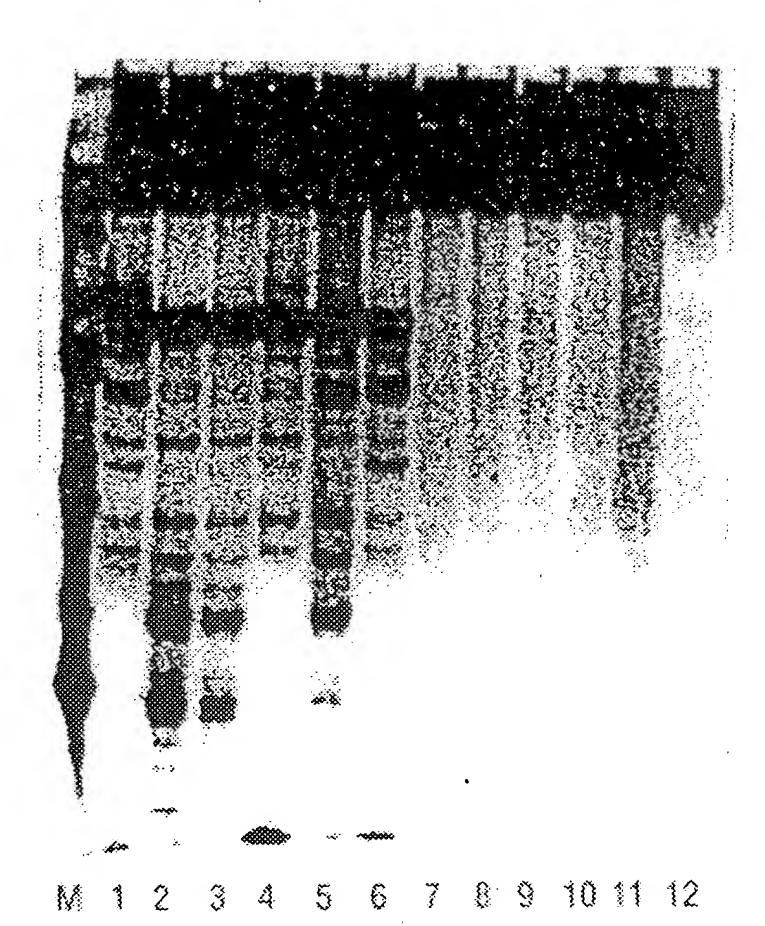
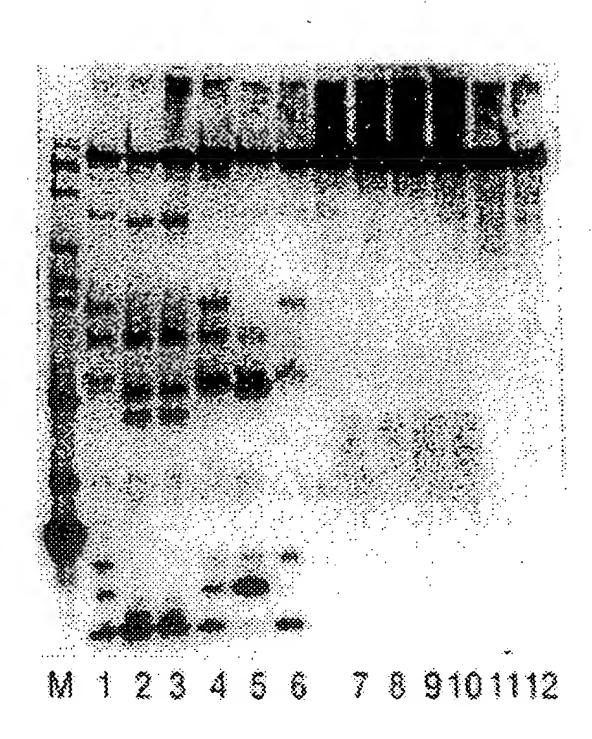


FIG. 50





FIC. 51



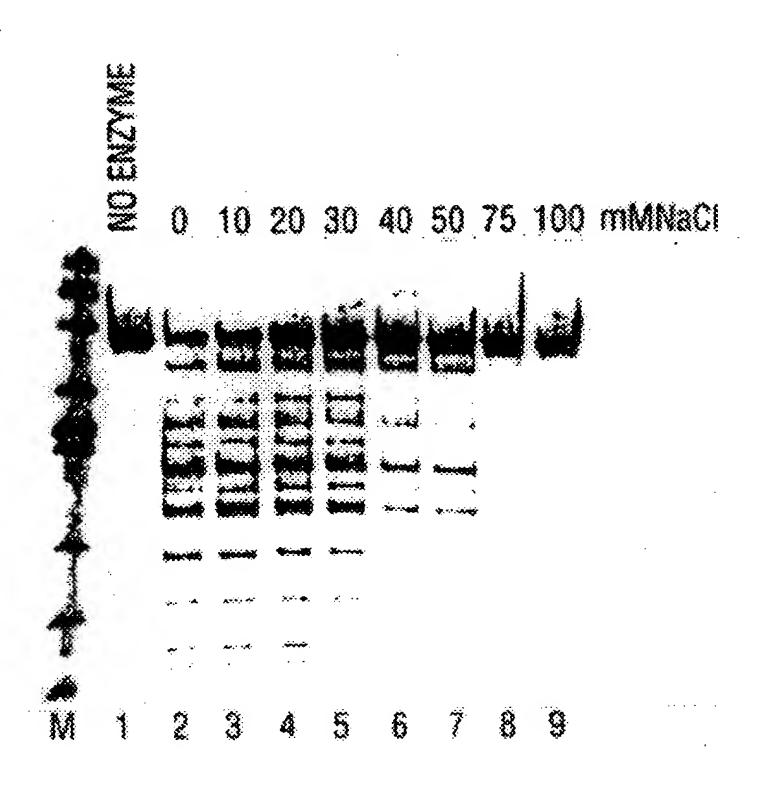


FIG. 52



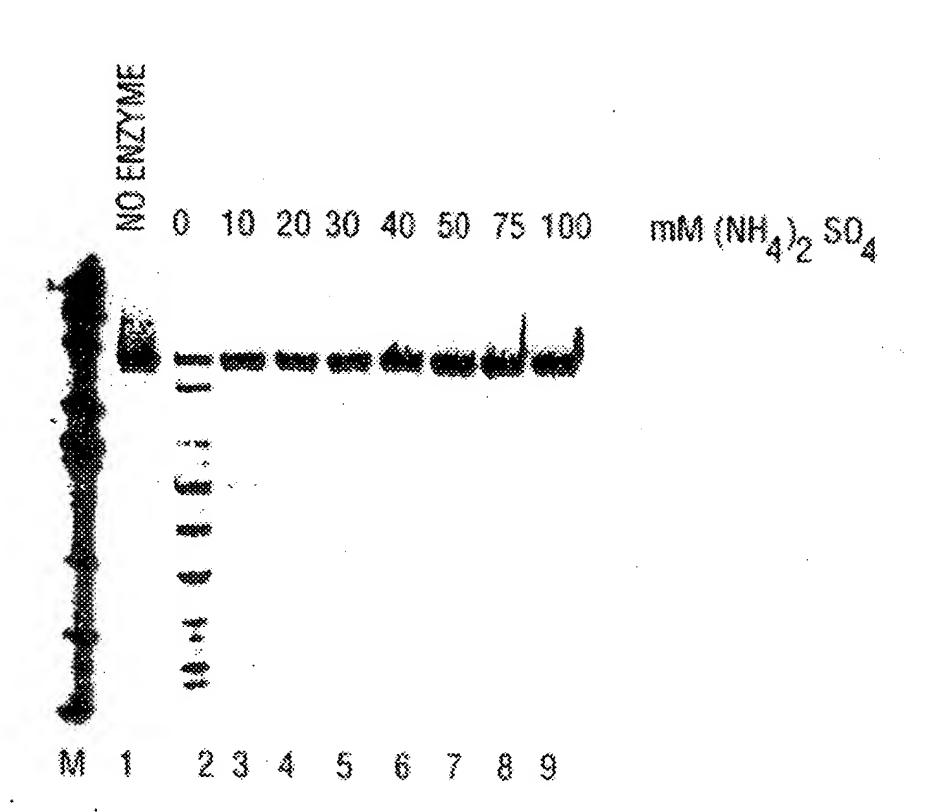


FIG. 53



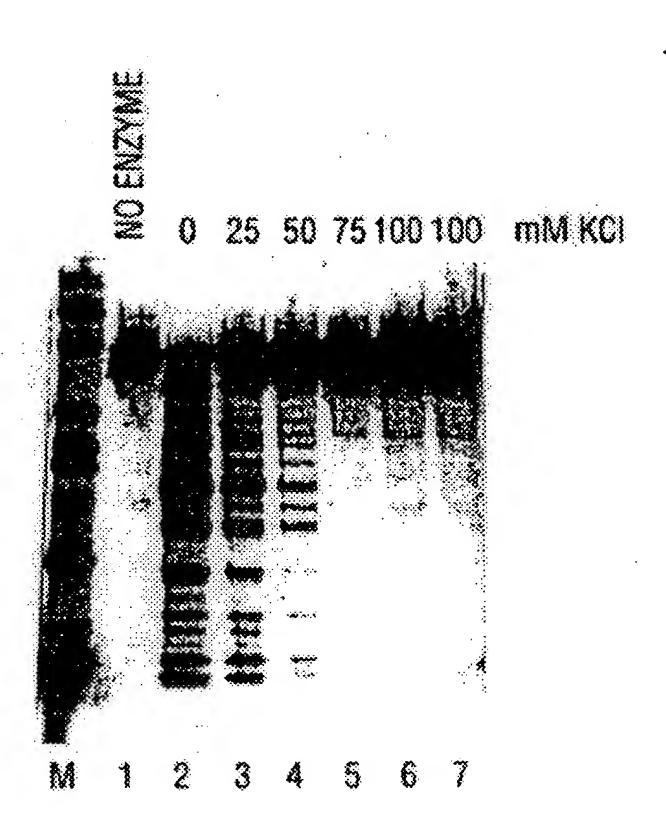


FIG. 54



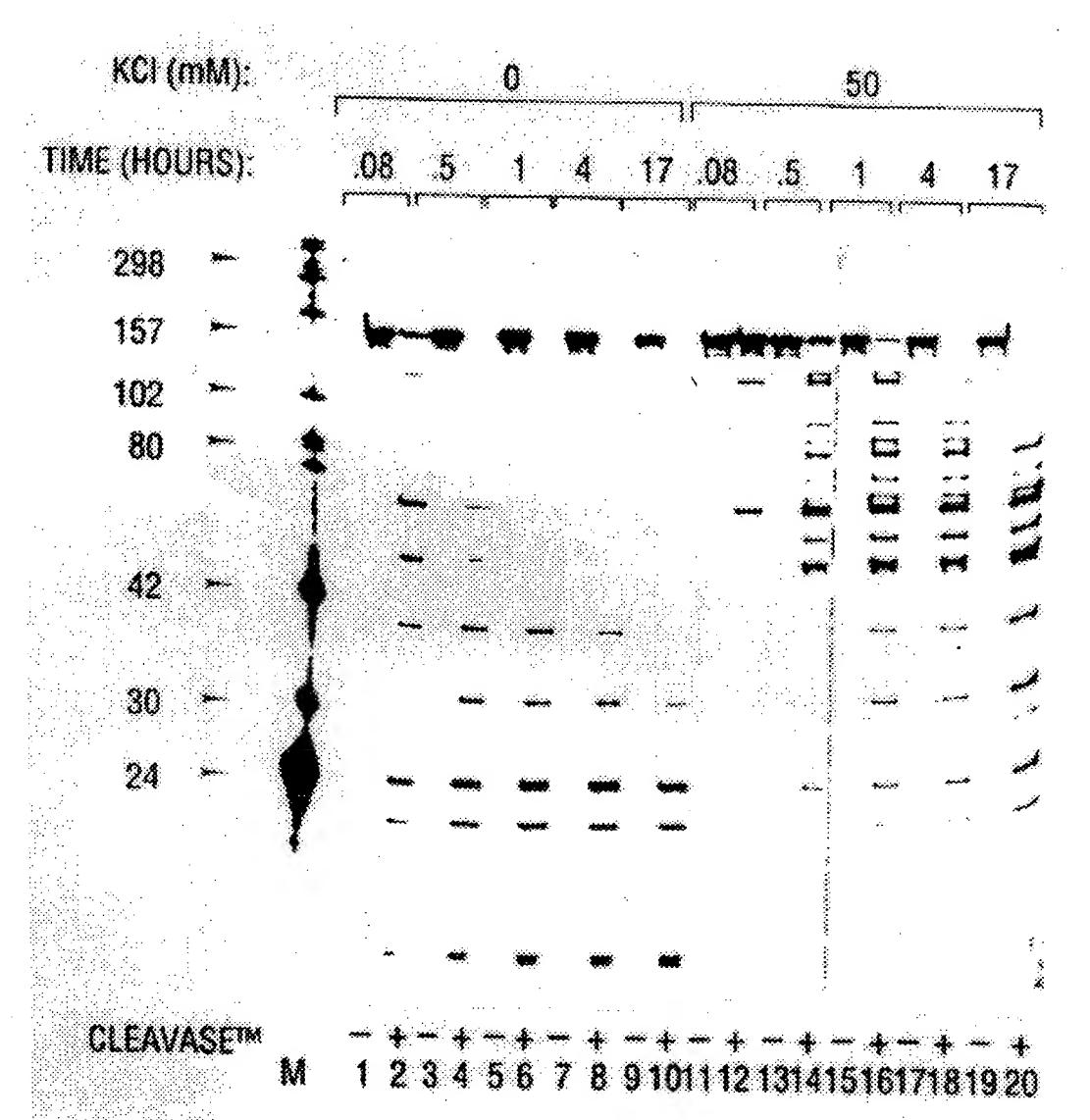


FIG. 55



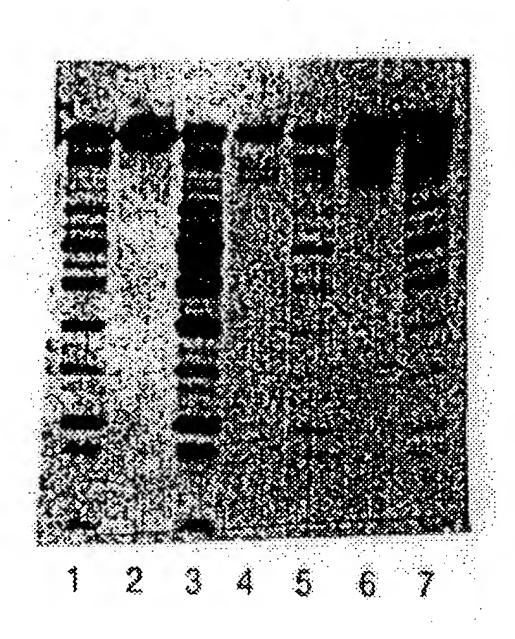


FIG. 56



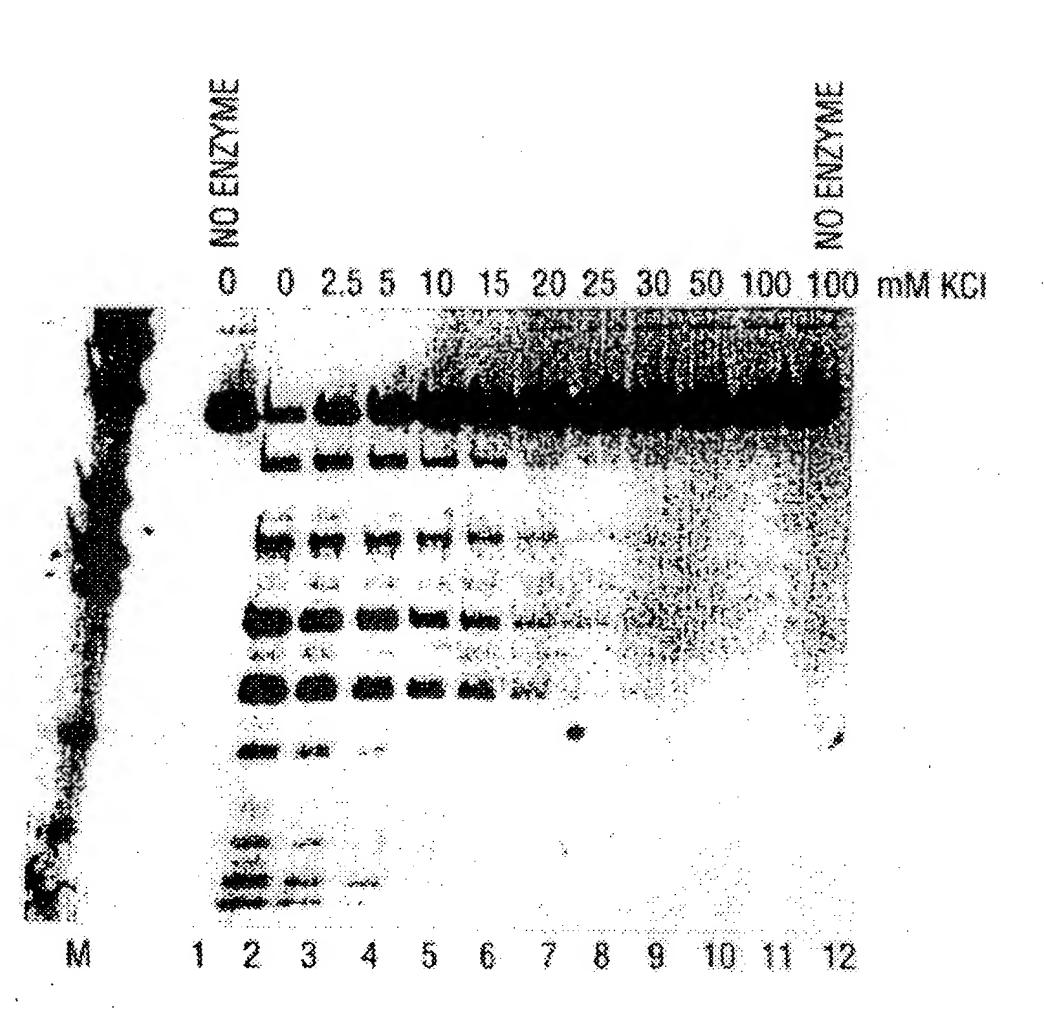


FIG. 57



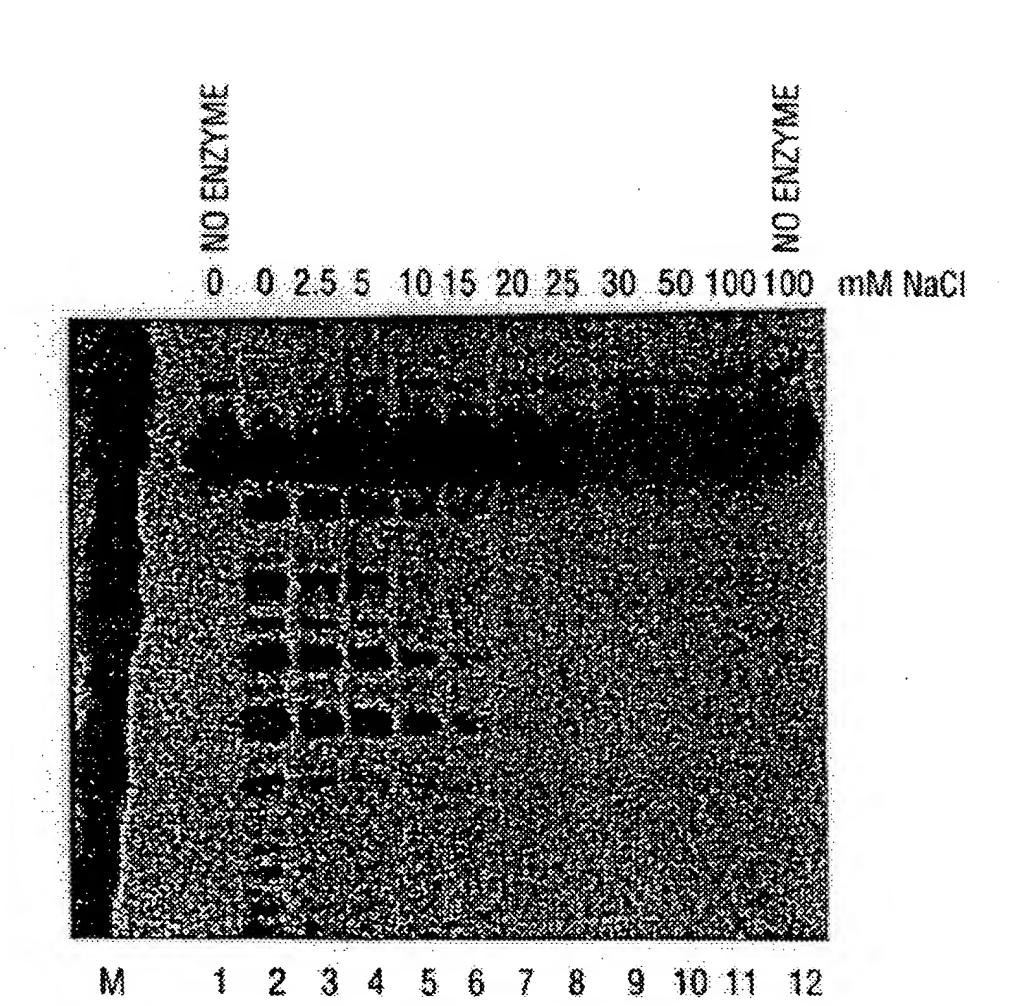


FIG. 58



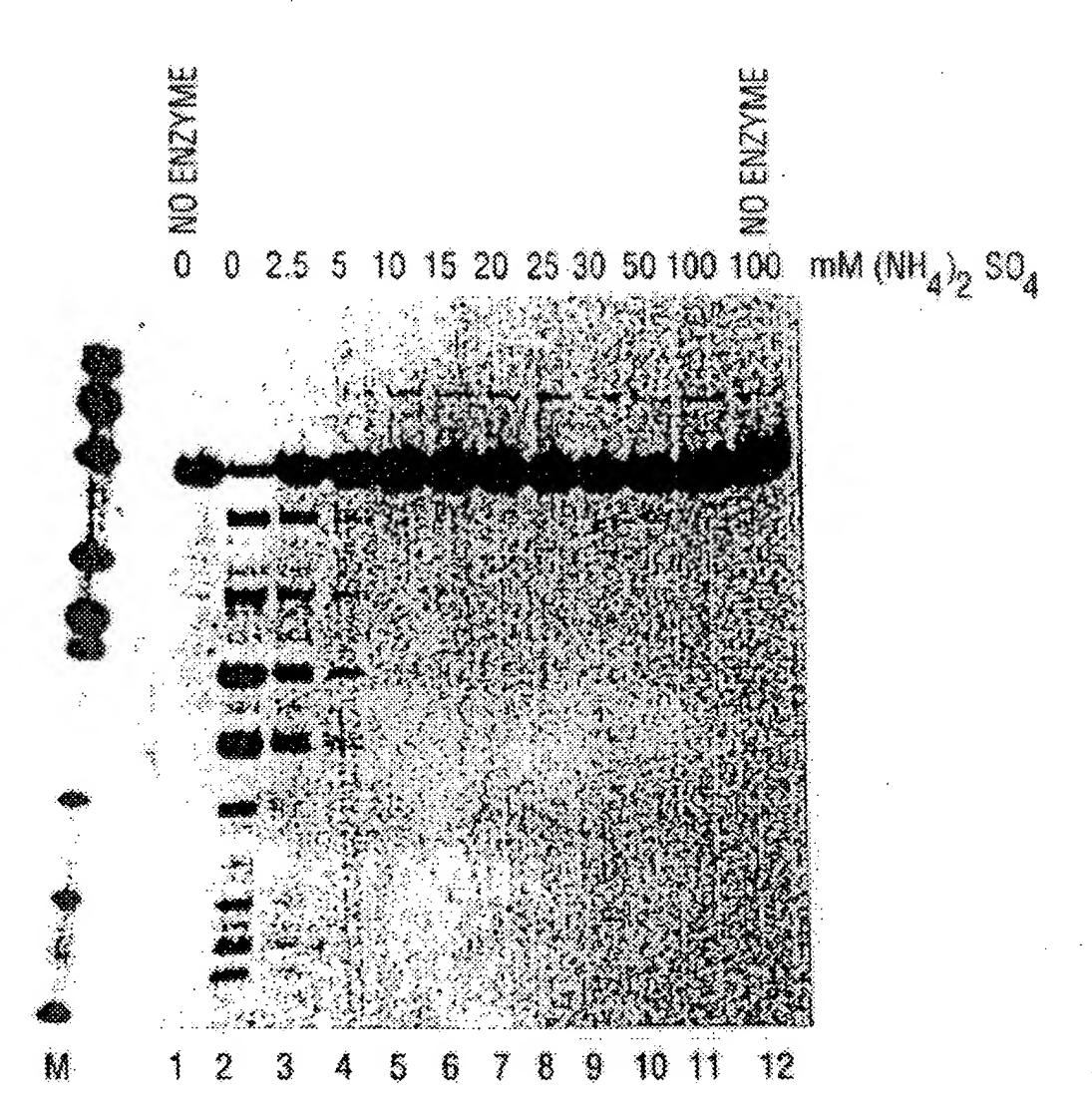


FIG. 59



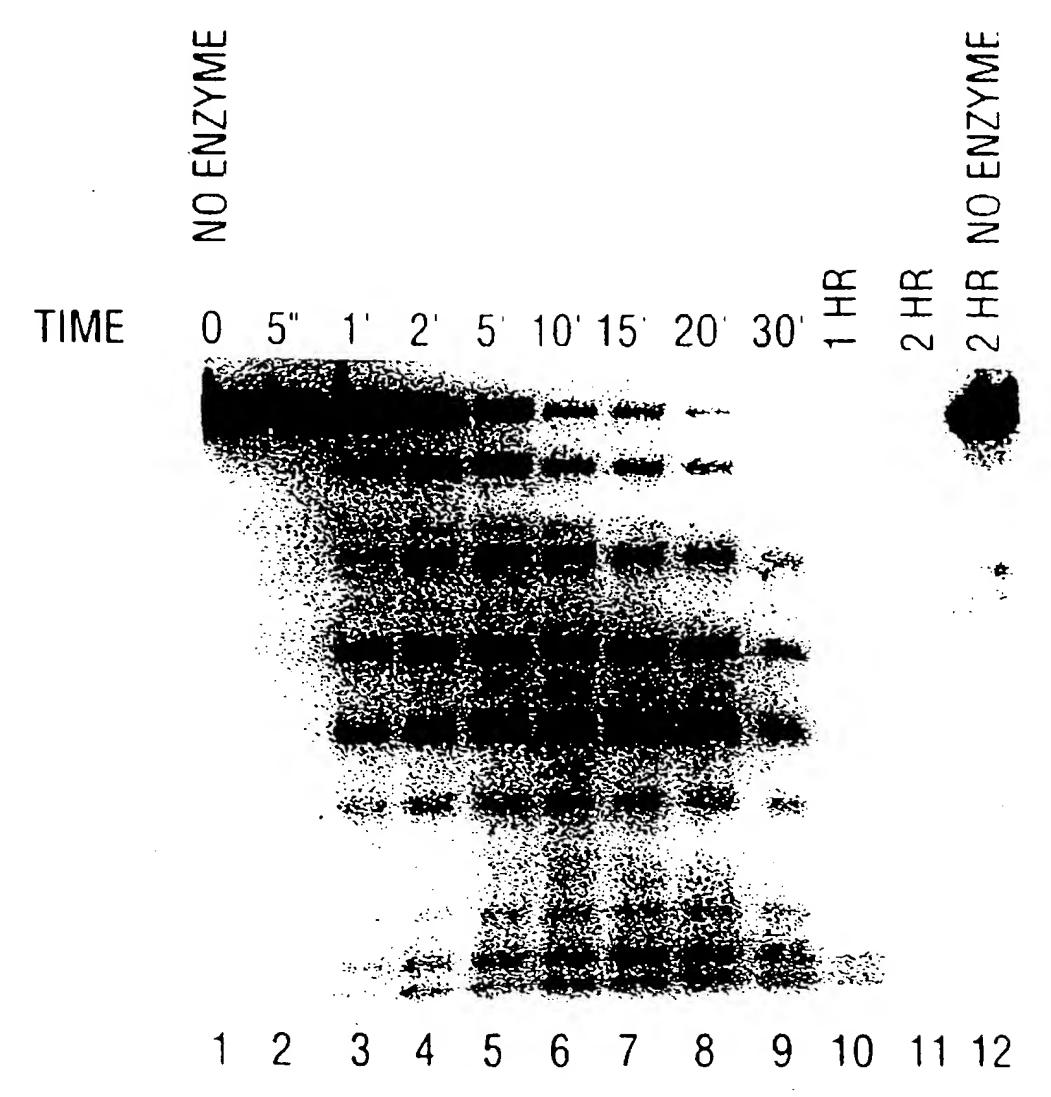
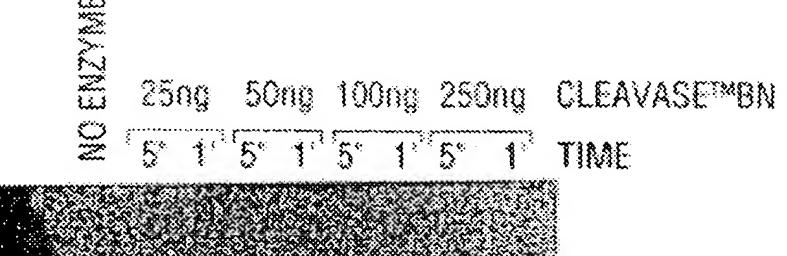


FIG. 60





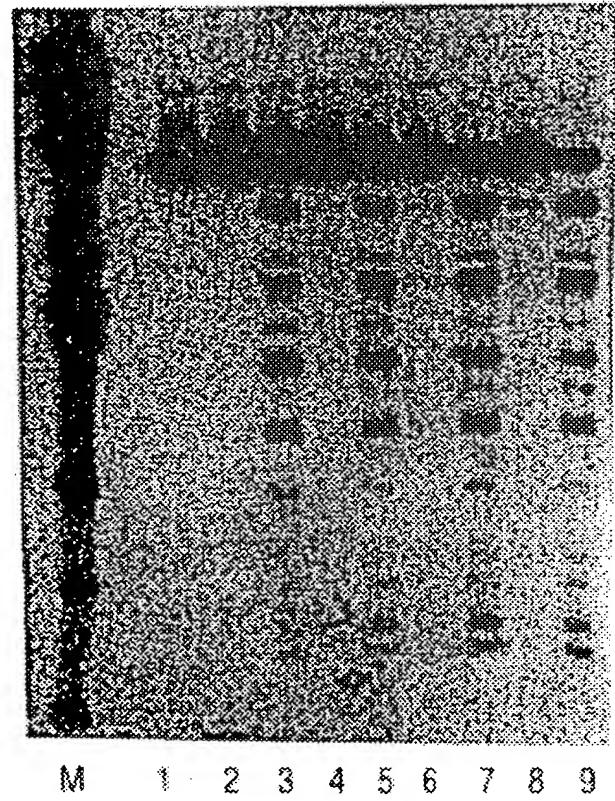


FIG. 61



37 37 37 40 45 50 55 60 65 70 75 80 80 80 TEMP. °C

FIG. 62



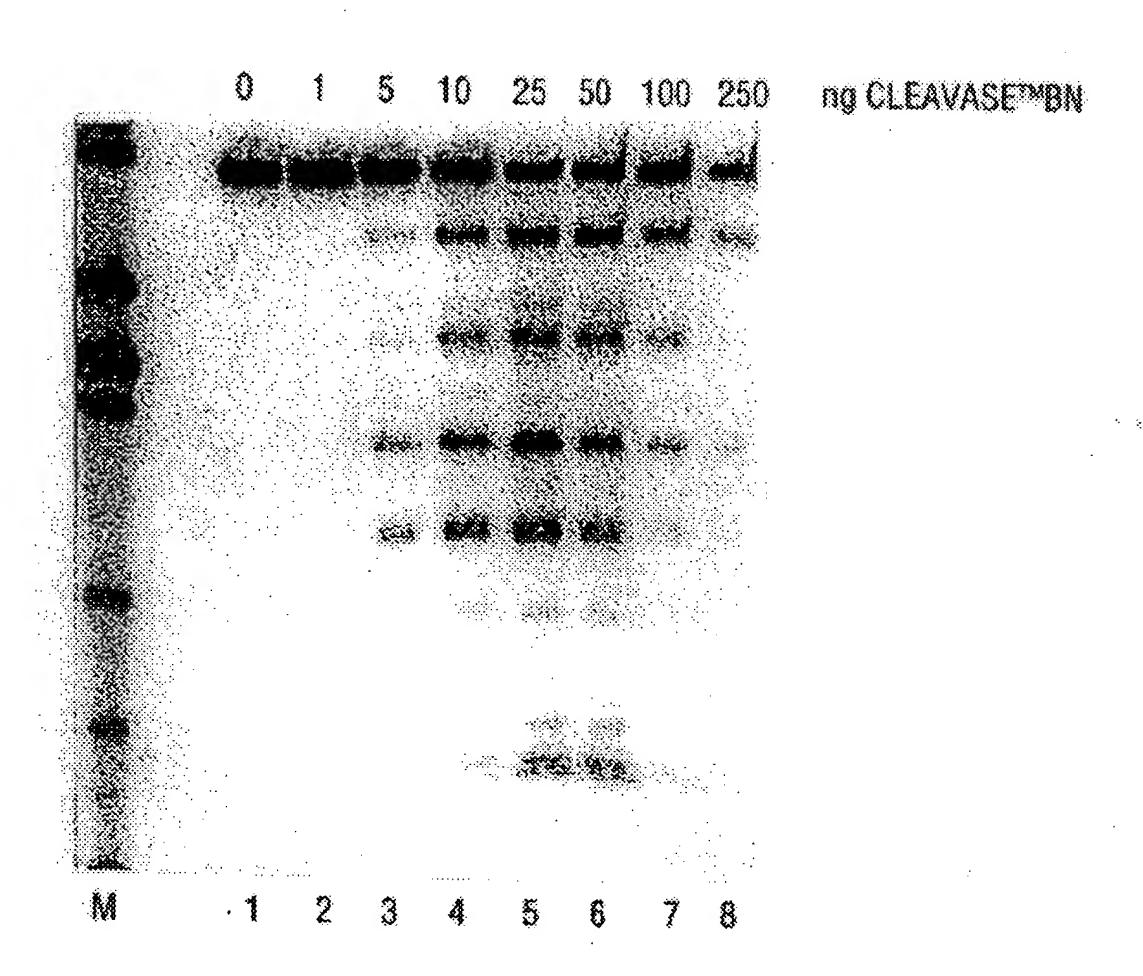
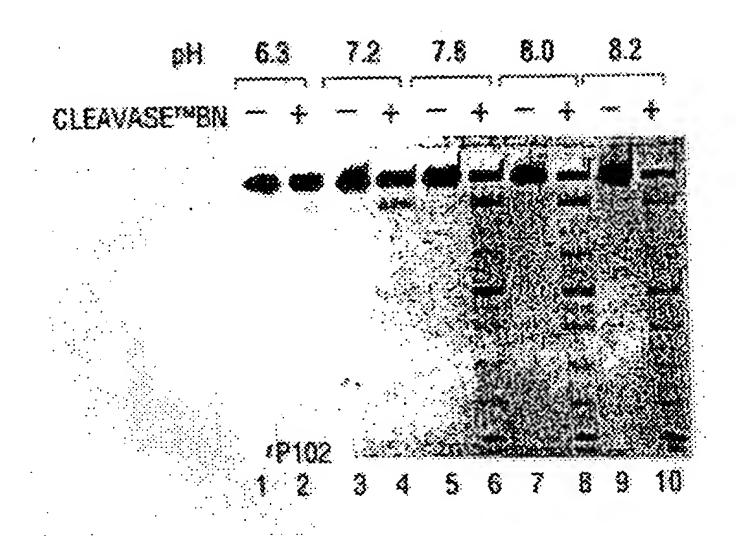


FIG. 63





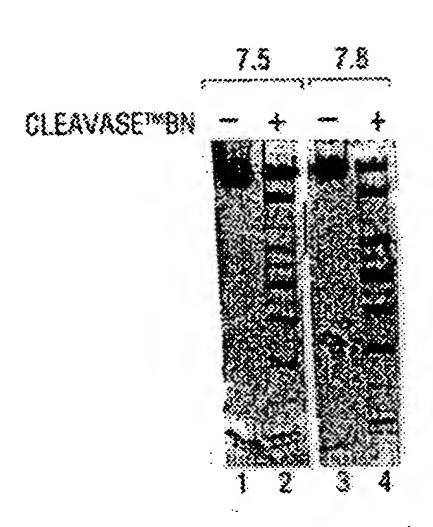


FIG. 64A

FIG. 64B



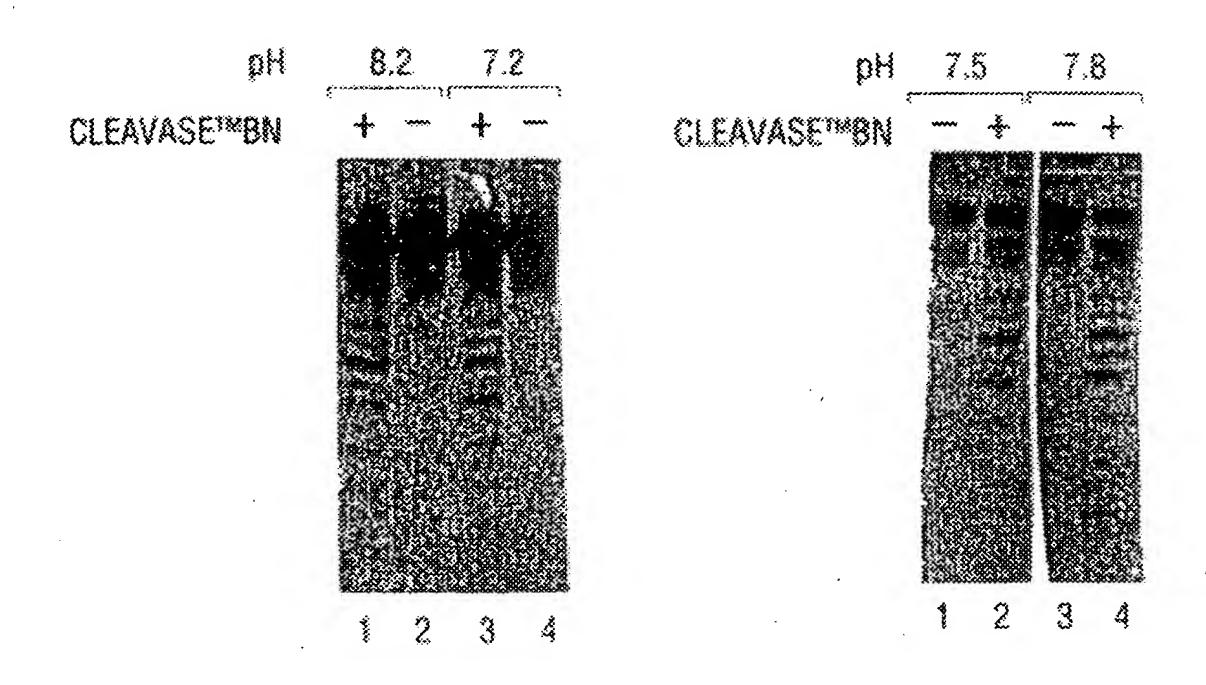


FIG. 65A

FIC. 65B



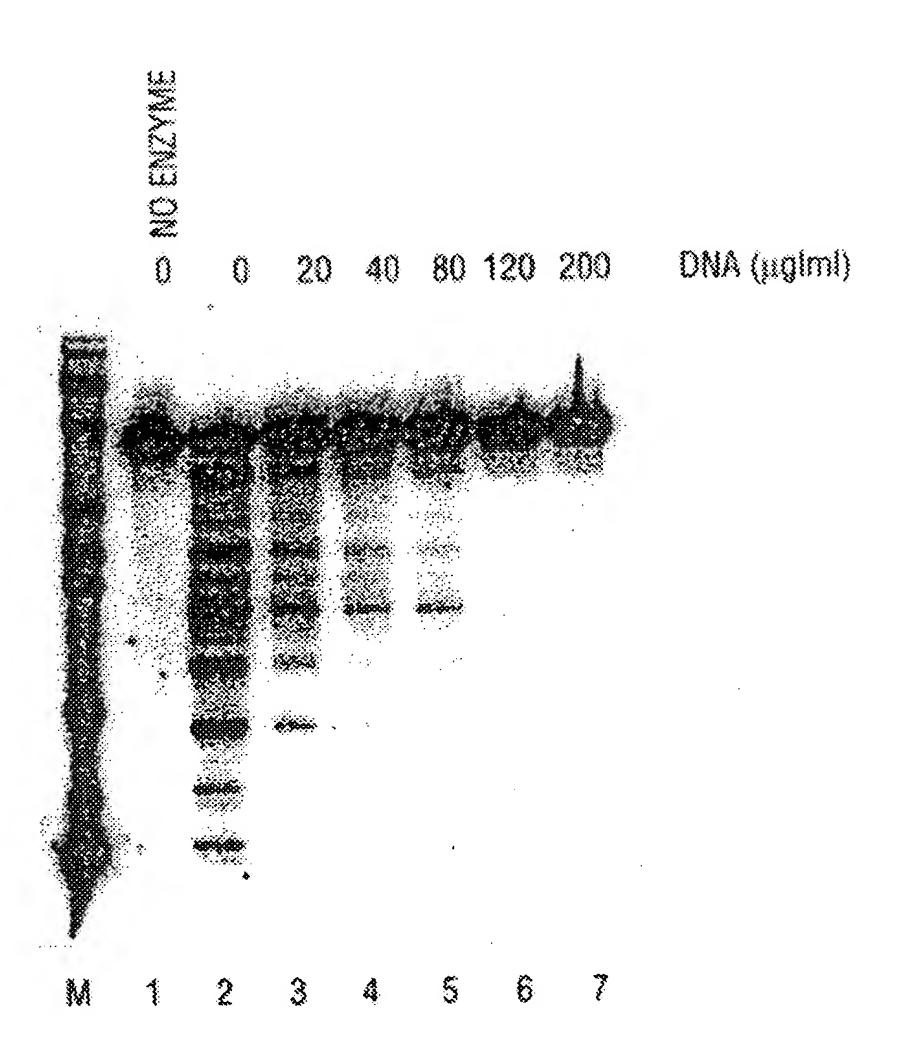


FIG. 66



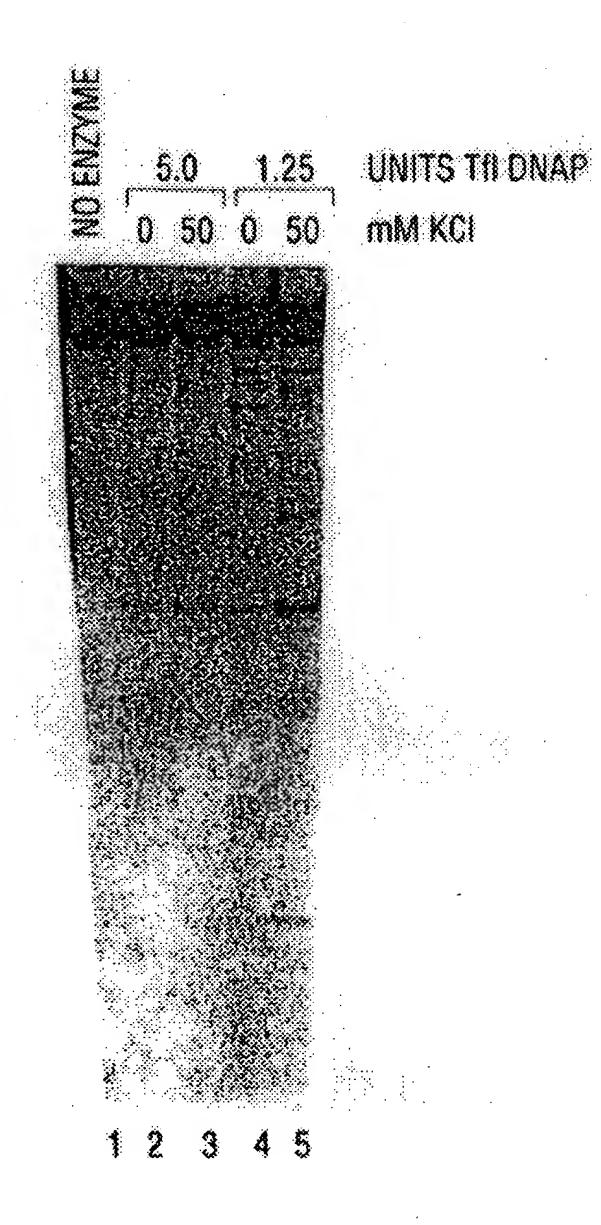


FIG. 67



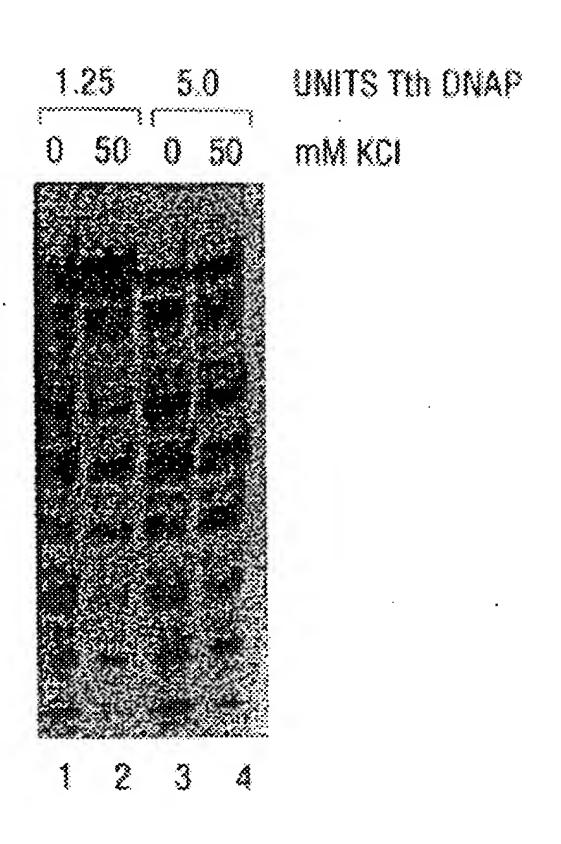


FIG. 68



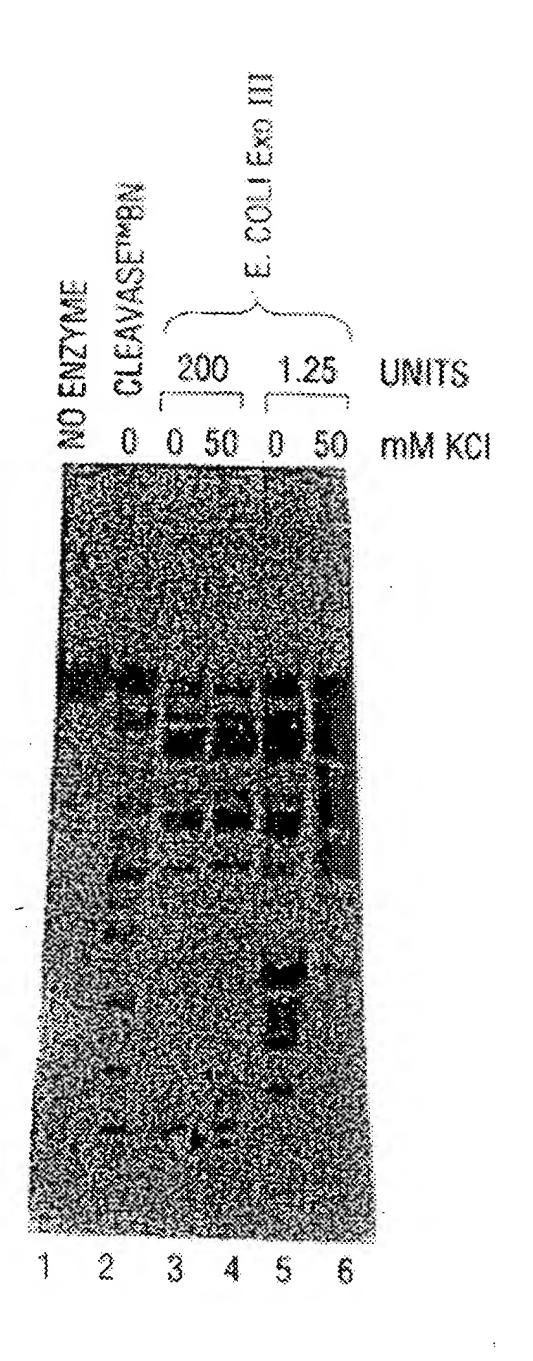


FIG. 69



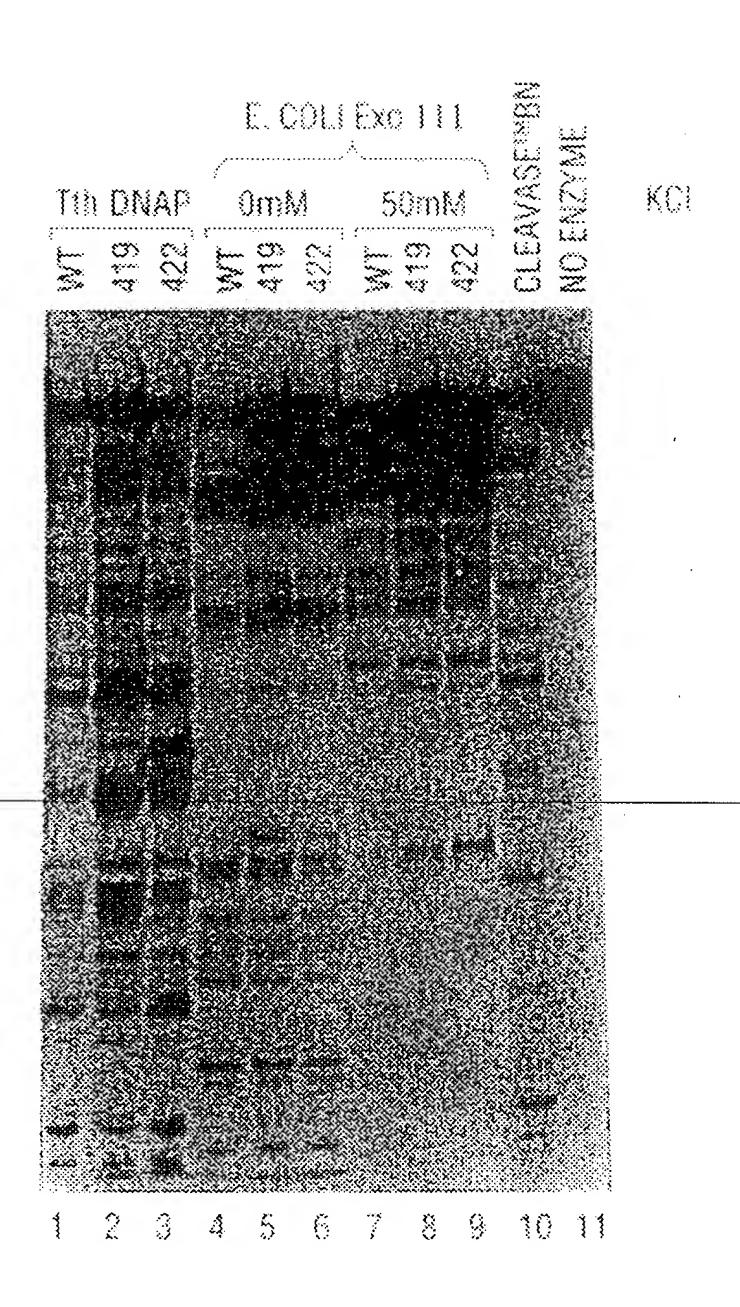
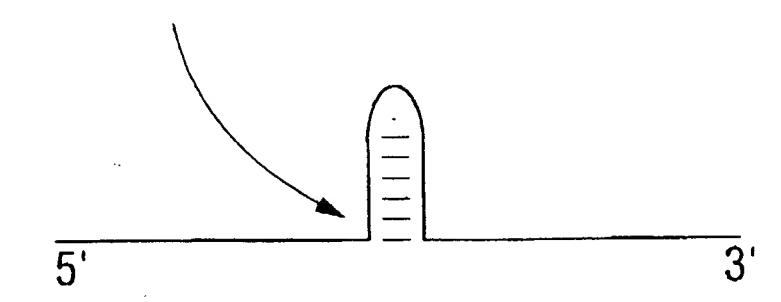


FIG. 70



## 5' CLEAVAGE SITE



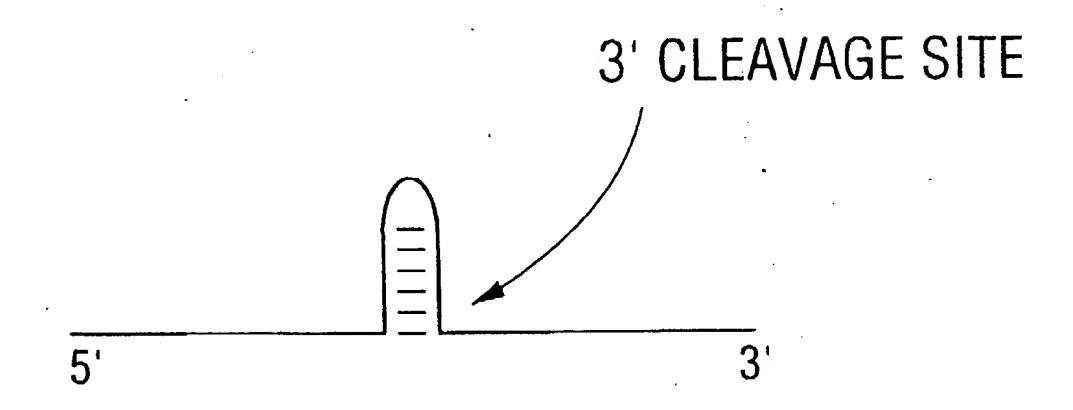


FIG. 71



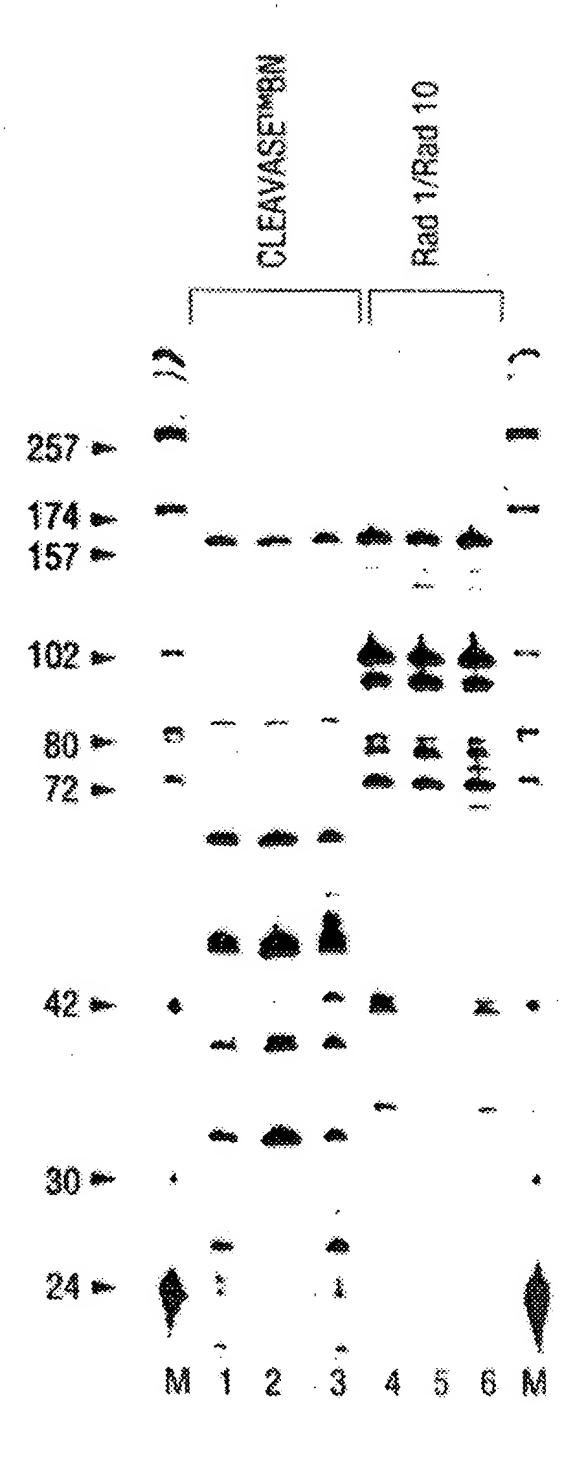
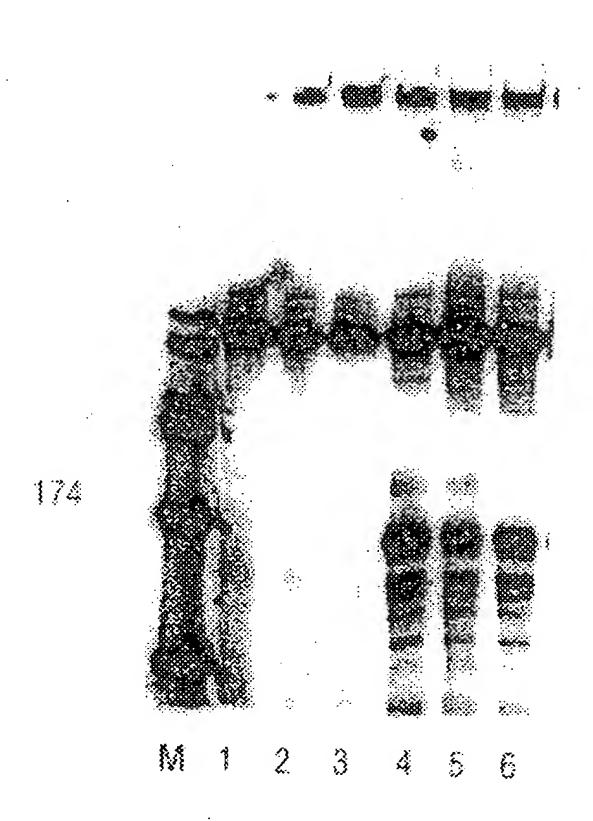


FIG. 72

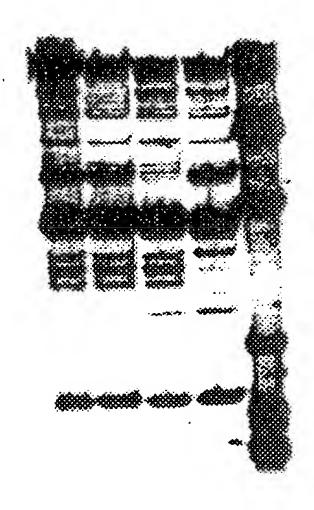




**"C.** 73



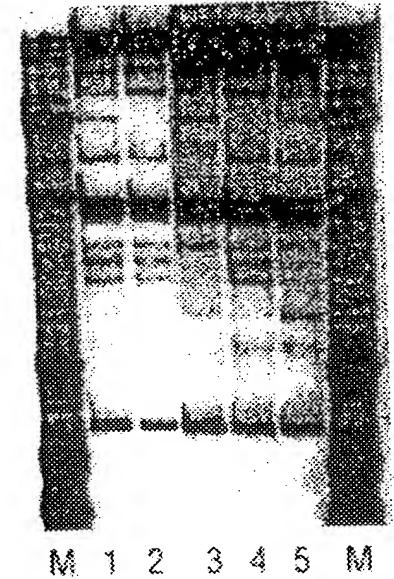
MUTANT WT 1 2 3



1234M

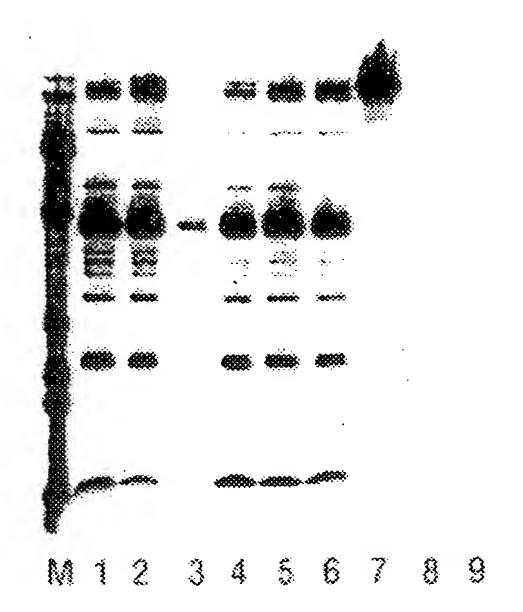
FIG. 74A

1SOLATE # 4 5 6 7 8



F(C. 745





FC. 75



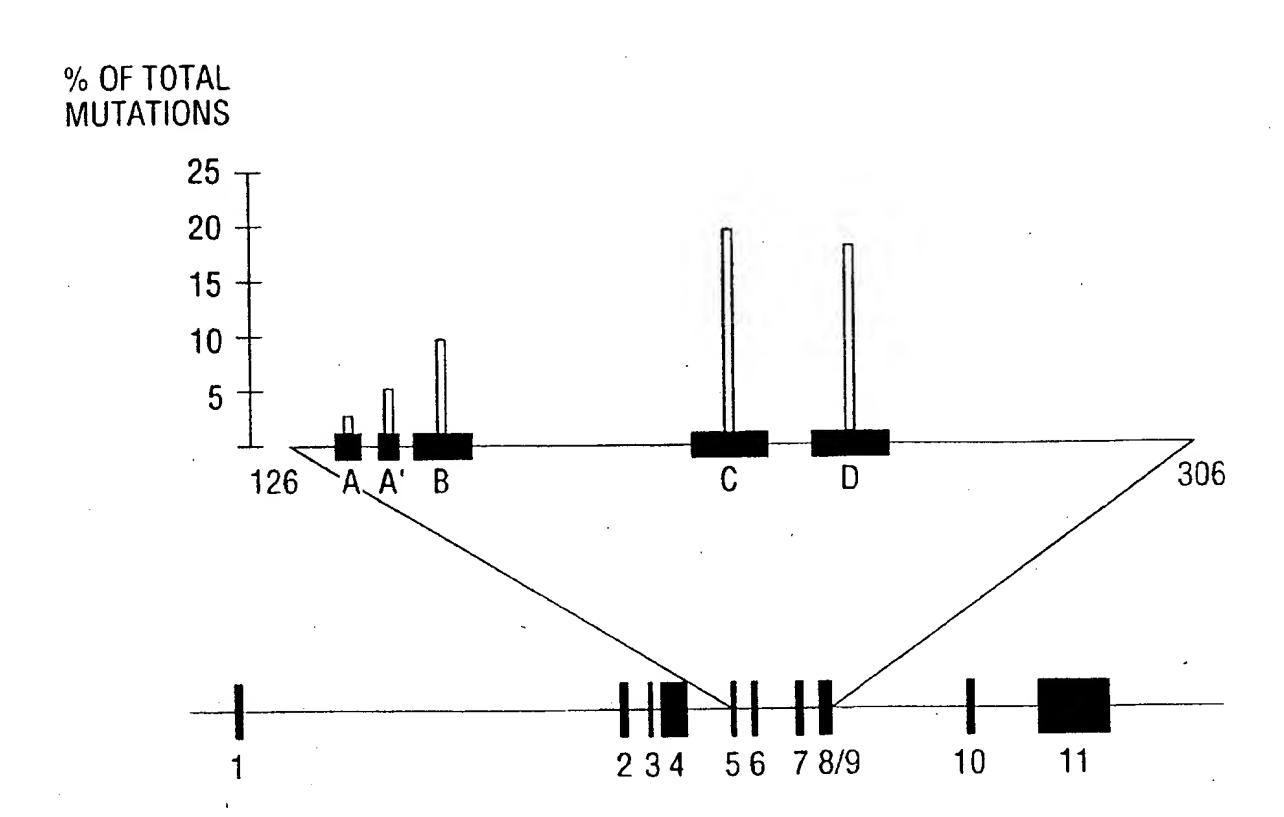


FIG. 76



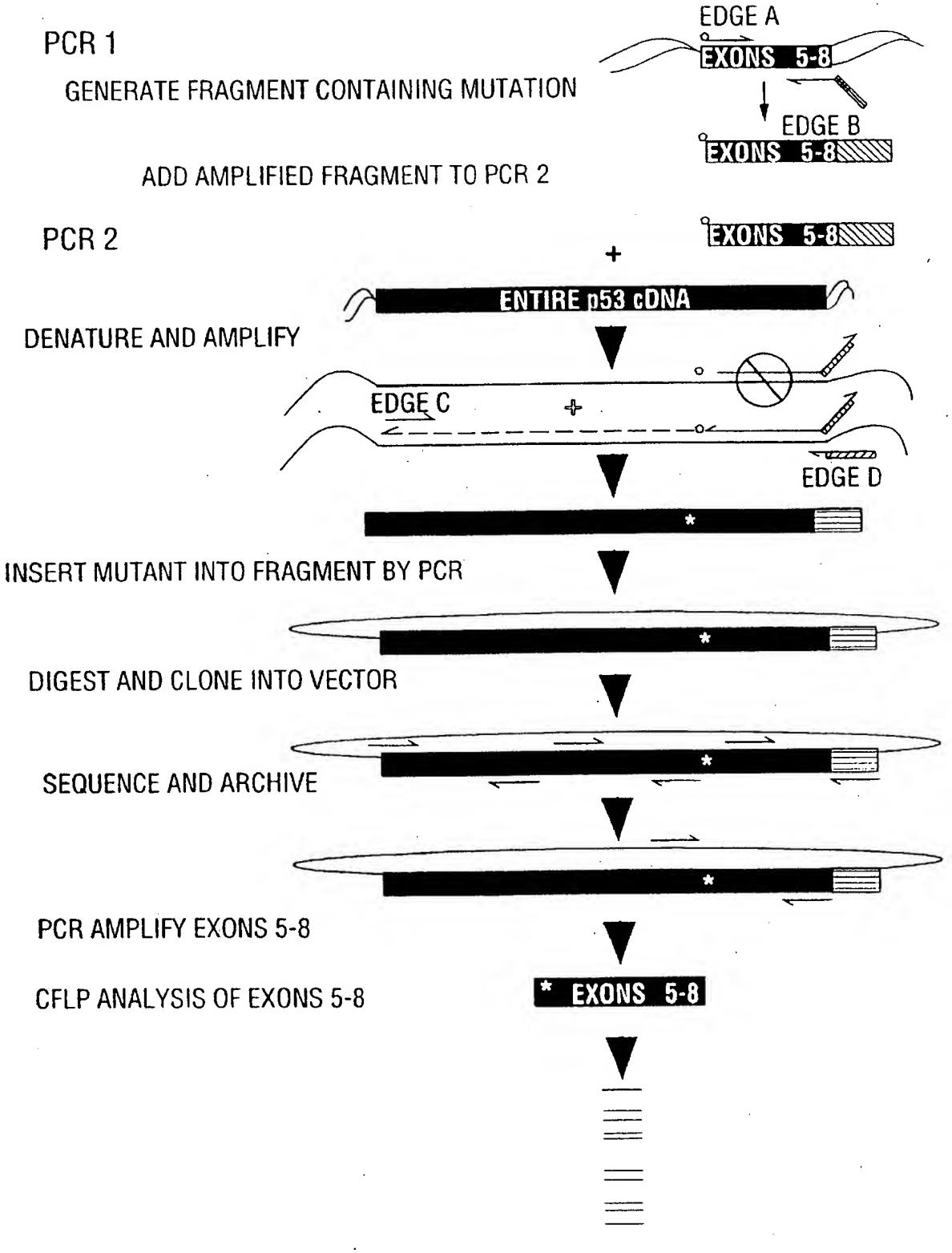


FIG. 77



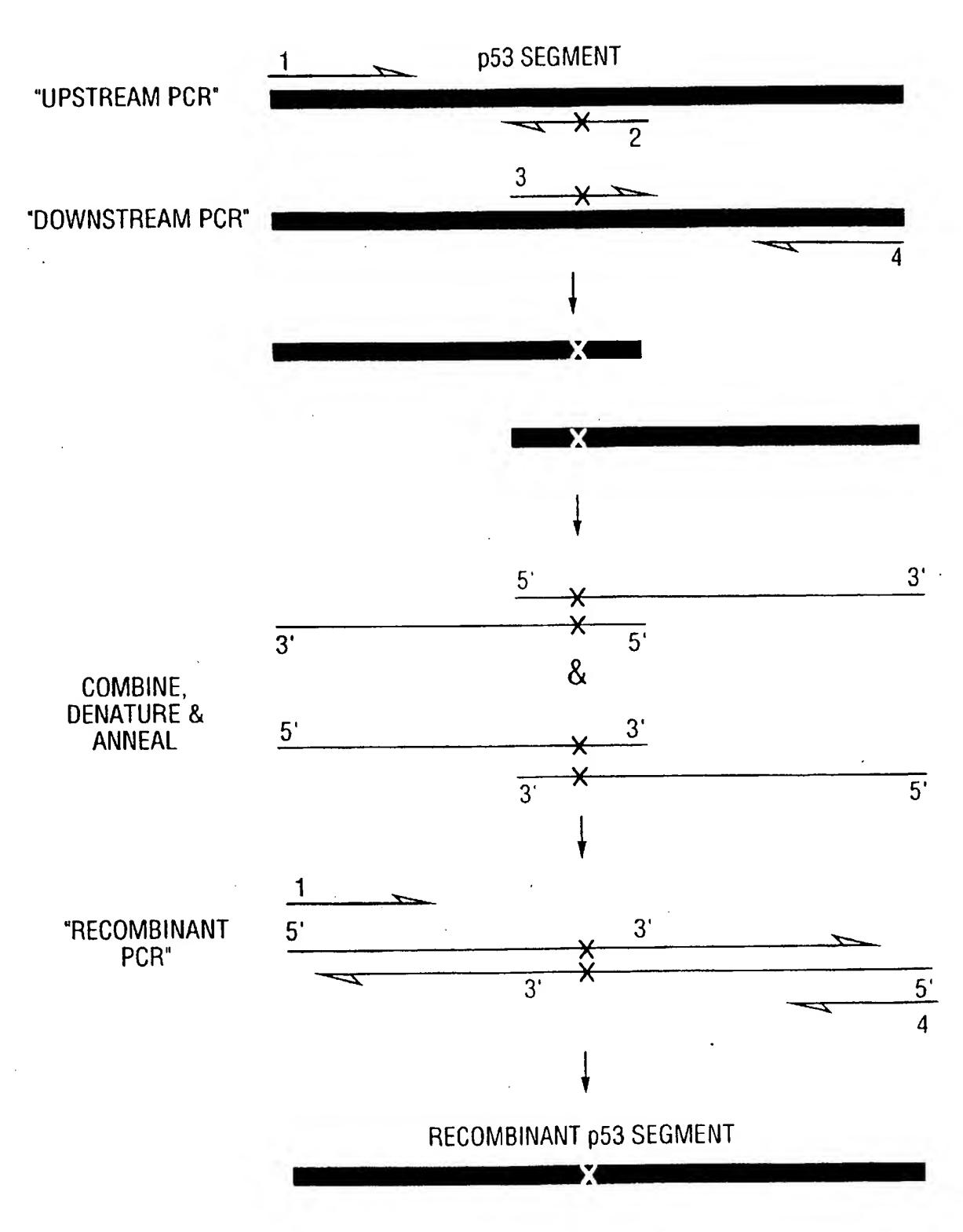
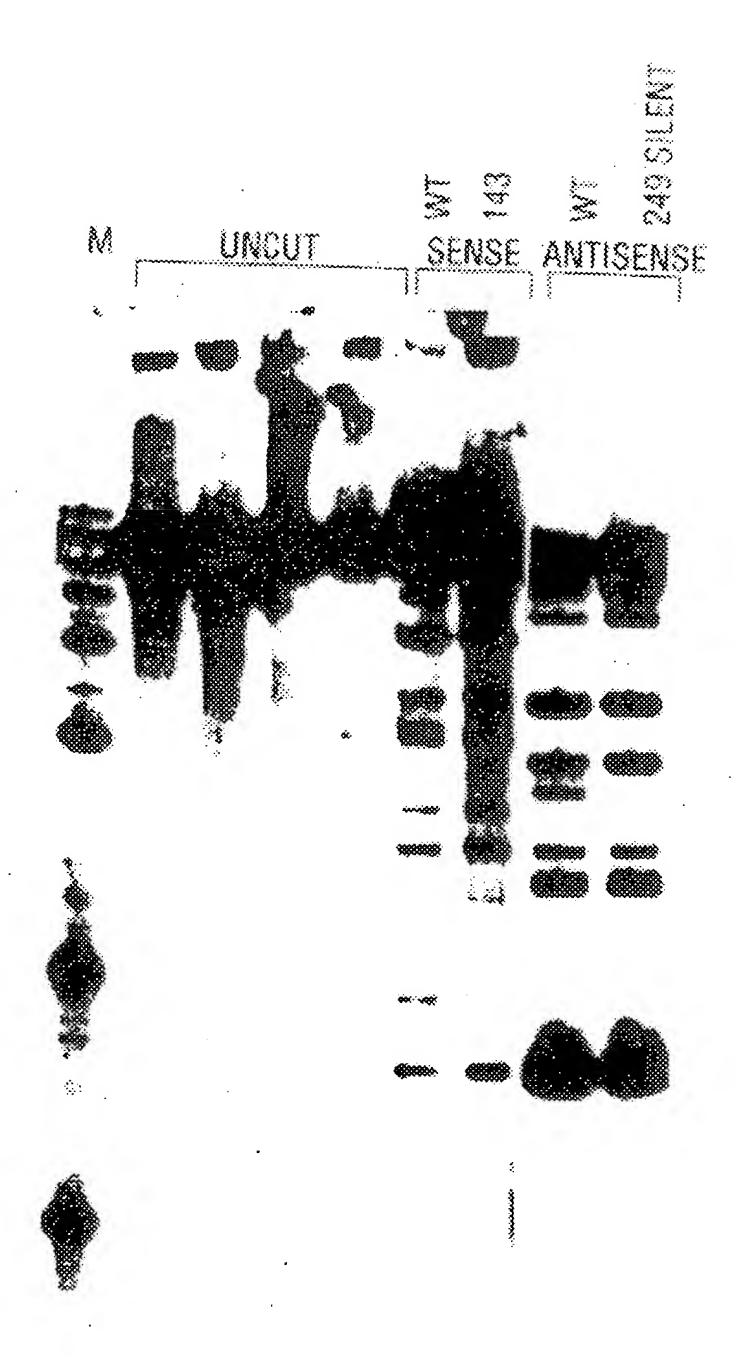


FIG. 78

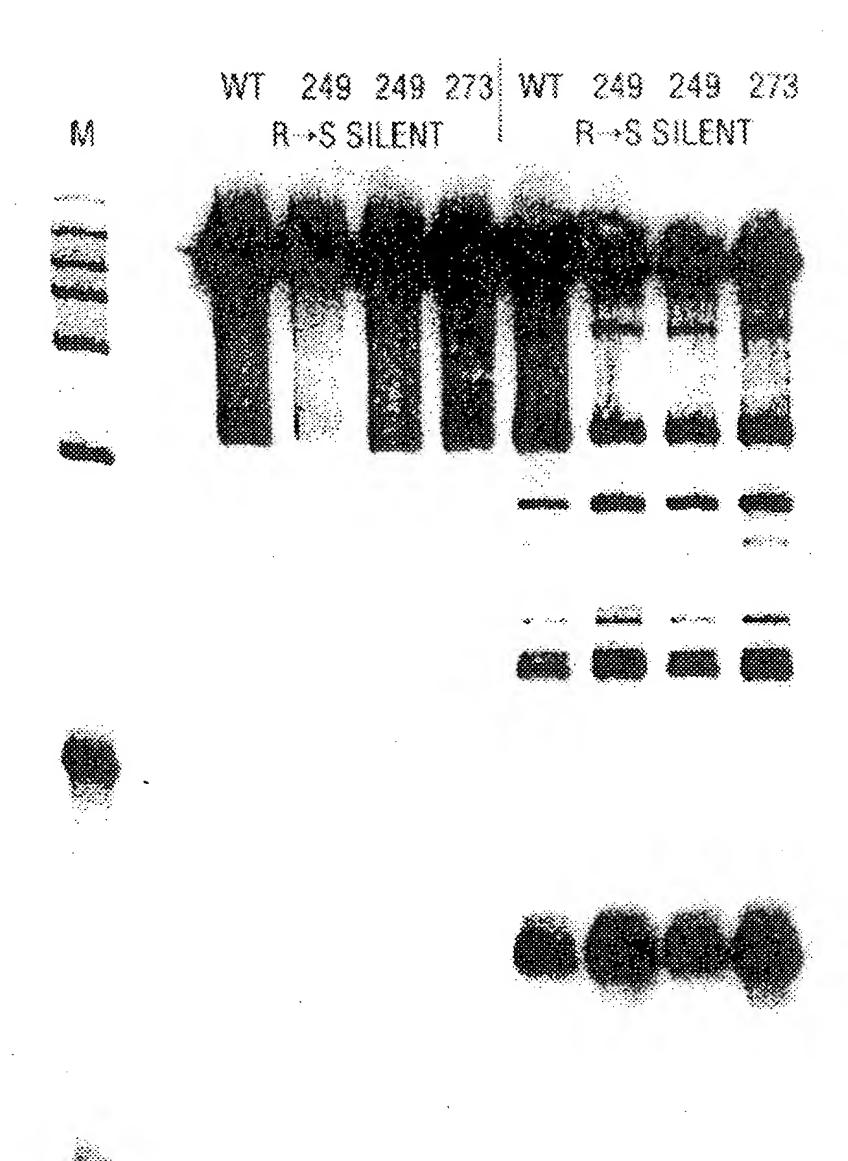




1 2 3 4 5 6 7. 8

FIG. 79





1 2 3 4 5 6 7 8



## MIXING PROPORTIONS

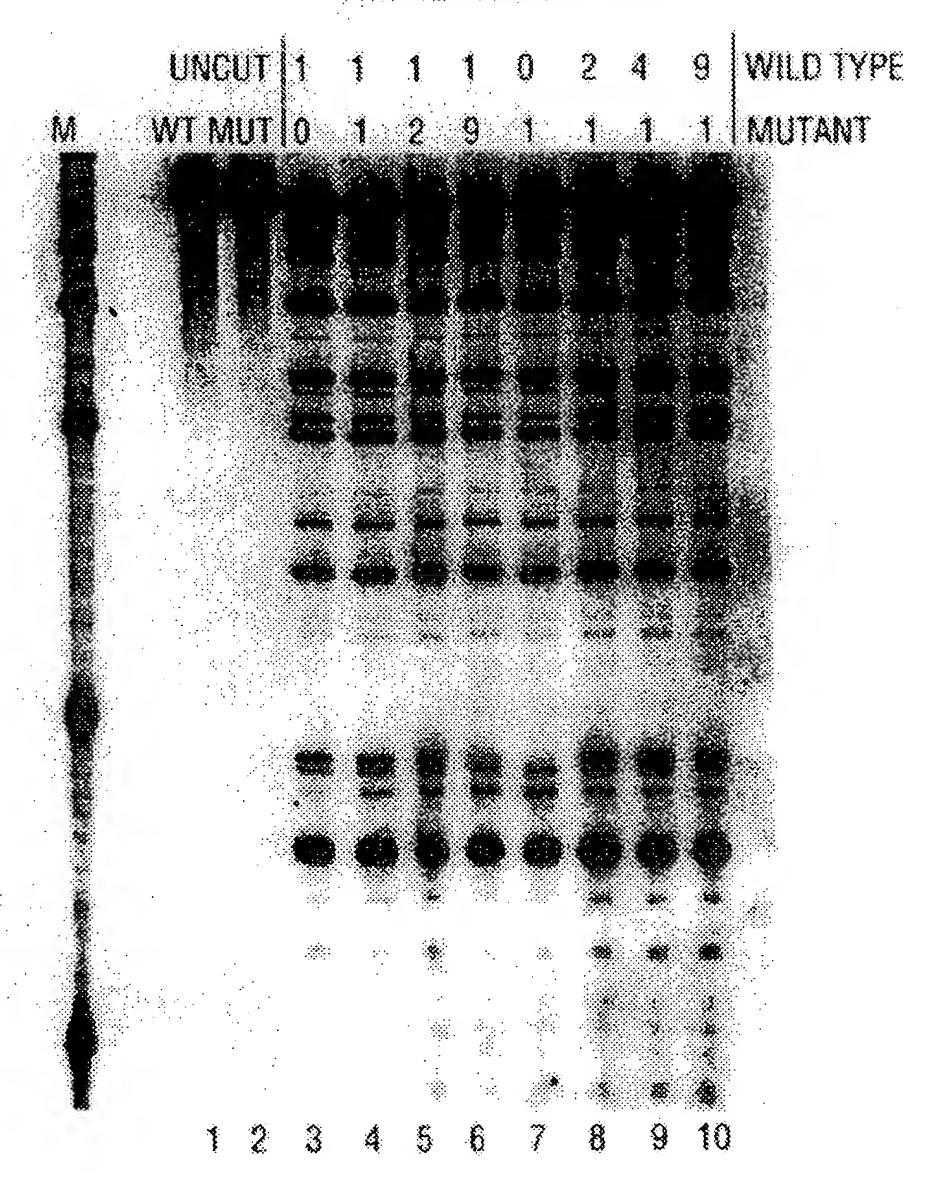


FIG. 81

. 05	100	150		•		•
GAGTGTCGTG GAGTGTCGTG GAGTGTCGTG GAGTGTCGTA GAGTGTCGTA GAGTGTCGTA	CTGCGGAACC CTGCGGAACC CTGCGGAACC CTGCGGAACC	TTGGAT-AAA TTGGAT-CAA TTGGAT-CAA	TGGAT-AA TGGA <u>G</u> -CA	·		
GCGTTAGTAT GCGTTAGTAT GCGTTAGTAT GCGTTAGTAT GCGTTAGTAT GCGTTAGTAT	CCATAGTGGT CCATAGTGGT CCATAGTGGT CCATAGTGGT CCATAGTGGT	GGGTCCTTTC GGGTCCTTTC GGGTCCTTTC	GGTCCTTT			
TCTGGCCATG TCTAGCCATG TCTAGCCATG TCTAGCCATG CCTAGCCATG	CCCGGGAGAG CCCGGGAGAG CCCGGGAGAG CCCGGGAGAG	CAGGACGACC CAGGACGACC CAGGACGACC	666AA6AC 6666TGAC	G. 82A		
GCAGAAAGCG GCAGAAAGCG GCAGAAAGCG GCAGAAAGCG GCAGAAAGCG	GACCCCCCCT GACCCCCCCT GACCCCCCCT GACCCCCCCT GACCCCCCCT	CCGGAATTGC CCGGAATTGC	CGGAATTG CGGAATCG			
CTGTCTTCAC CTGTCTTCAC CTGTCTTCAC CTGTCTTCAC CTGTCTTCAC	CAGCCTCCAG CAGCCTCCAG CAGCCTCCAG CAGCCTCCAG	GGTGAGTACA GGTGAGTACA GGTGAGTACA	GTGAGTAC GTGAGTAC			•
<b></b>	51	101				
ID NO:121) ID NO:122) ID NO:123) ID NO:124) ID NO:125) ID NO:125)						
(SEQ (SEQ (SEQ (SEQ (SEQ	•					
HCVI.1 HCV2.1 HCV3.1 HCV4.2 HCV6.1	HCV1.1 HCV2.1 HCV3.1 HCV4.2 HCV6.1	HCV1.1 HCV2.1 HCV3.1	CV4 CV6. CV7.	· .	•	



151 CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG 200 CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCGAGA CTGCTAGCCG CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCGAGA CTGCTAGCCG CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG CCCACTCLAT GCCCGGGCCAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG	201 AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCCT 25 AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT AGTAGCGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT AGTAGCGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT	251 GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC 282 GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC
HCV1.1	HCVI.1	HCVI.1
HCV2.1	HCV2.1	HCV2.1
HCV3.1	HCV3.1	HCV3.1
HCV6.1	HCV6.1	HCV4.2
HCV6.1	HCV6.1	HCV6.1

FIG. 82B



SENSE

ANTISENSE

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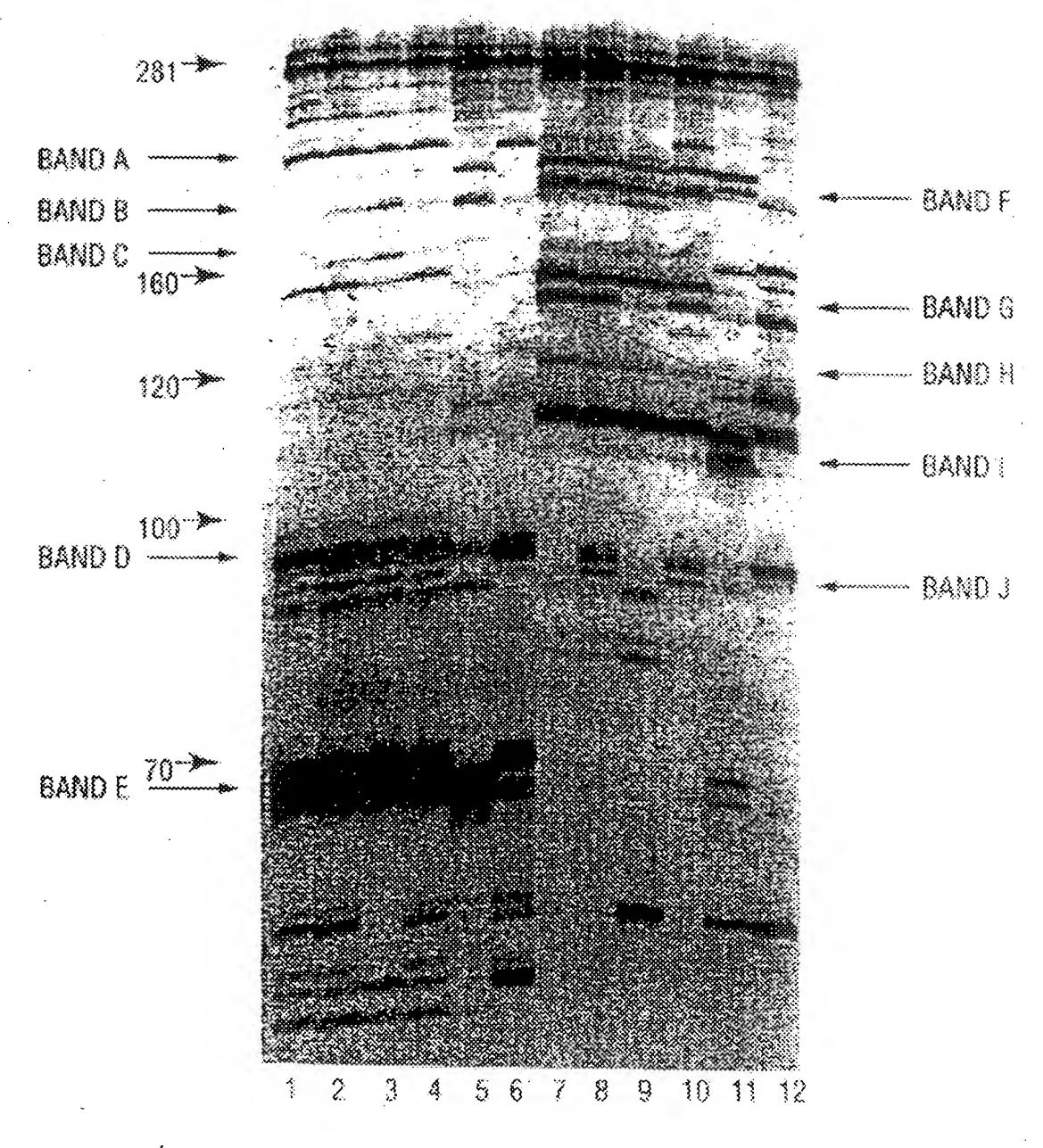


FIG. 83



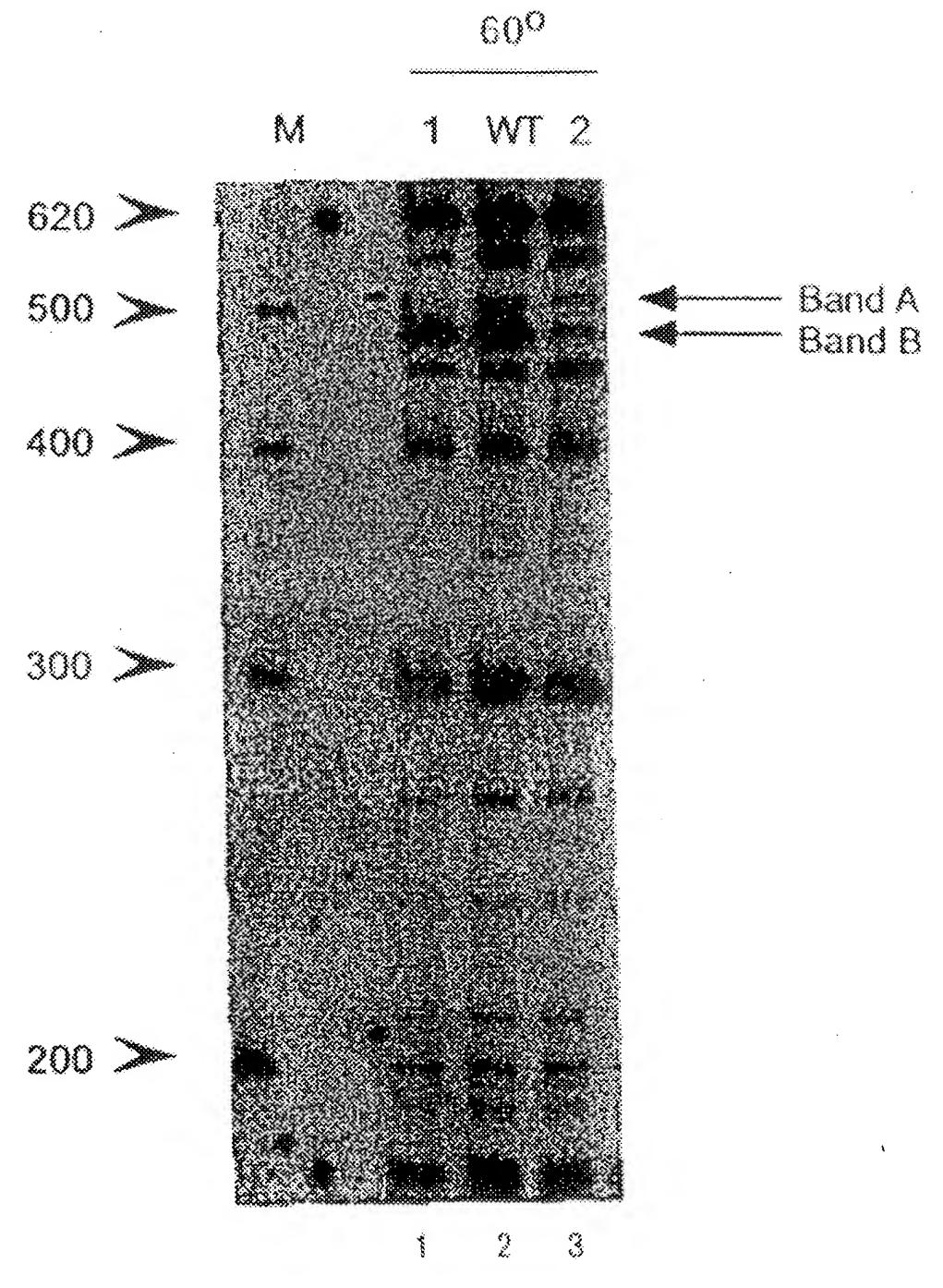
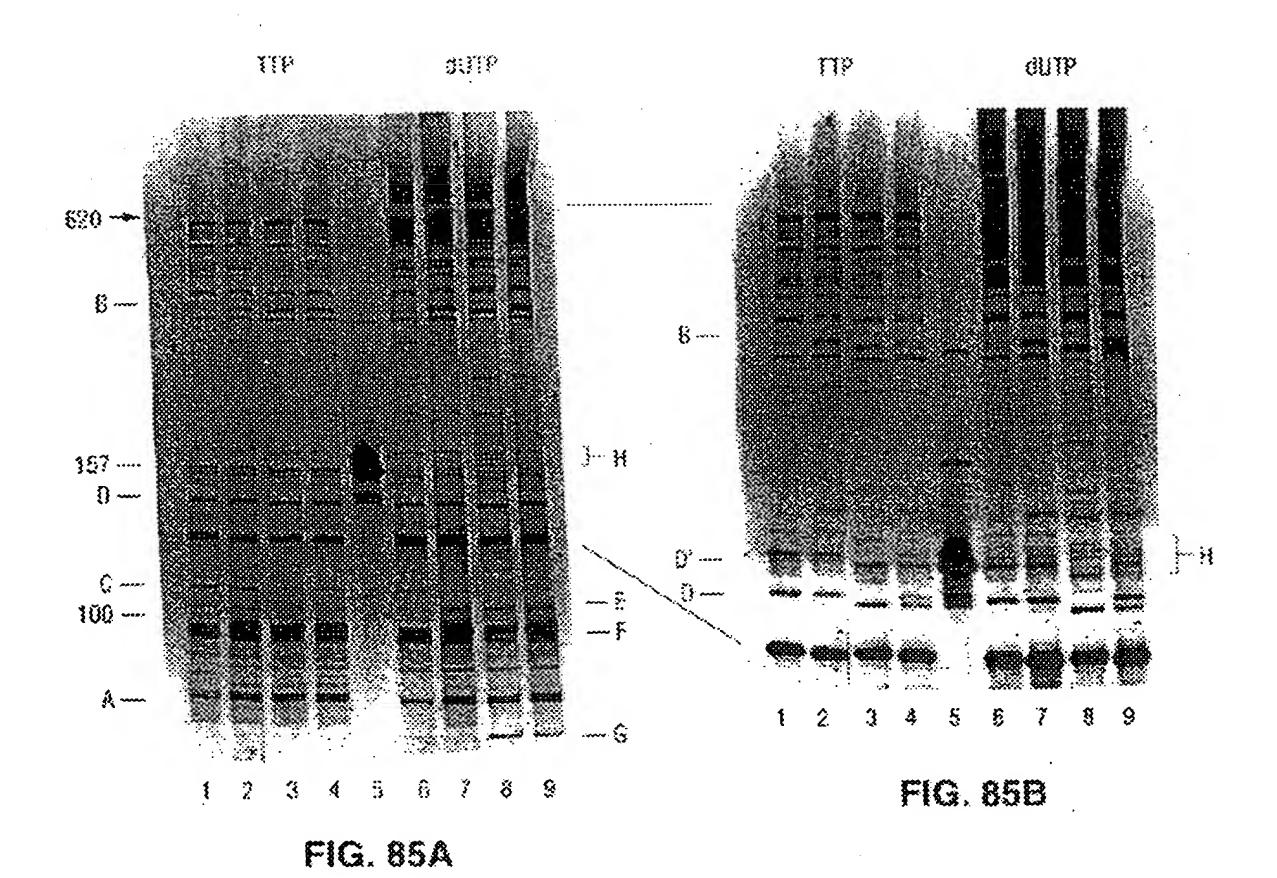


FIG. 84





## SENSE STRAND

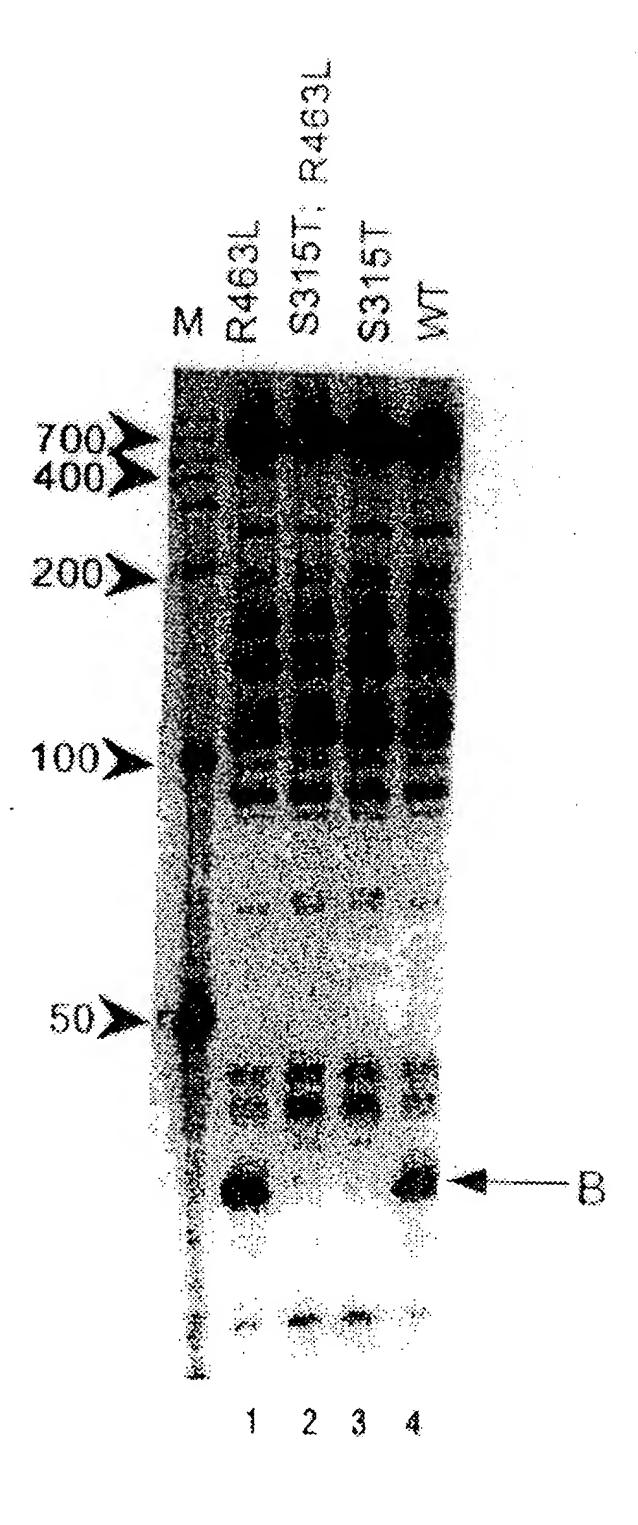
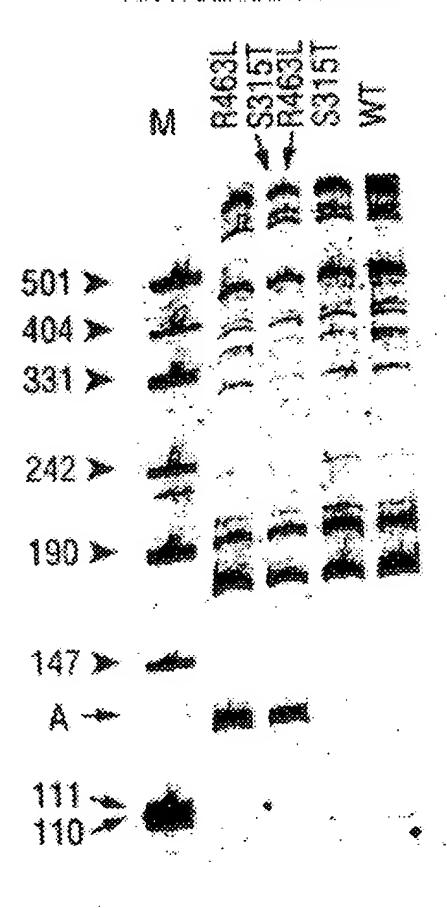


FIG. 86



## ANTISENSE STRAND



1 2 3 4

FIG. 87

MAR 1 9 2004	1638		01.01	<b>_</b>				1659
	09	ACACATGCAA TGTGTACGTT		GGGTGAG CCCACTC	180 AATACCGCAT TTATGGCGTA	240 TGCCCAGATG ACGGGTCTAC	300 TGGTCTGAGA ACCAGACTCT	360 GCAGCAGTGG CGTCGTCACC CGTCGTC
	20	GGCAGGCCTA CCGTCCGGAT	110	AGTGGCGGAC TCACCGCCTG	170 AACGGTAGCT TTGCCATCGA	CCATCGGATG GGTAGCCTAC	290 GATCCCTAGC CTAGGGATCG	350 CCTACGGGAG GGATGCCCTC GGATGCCCTC
	40	GAACGCTGGC CTTGCGACCG	100	TTTGCTGACG AAACGACTGC	160 AACTACTGGA TTGATGACCT	220 GGCCTCTTG CCCGGAGAAC	280 CCTAGGCGAC GGATCCGCTG	340 GGTCCAGACT CCAGGTCTGA TGA
	30 <b>GCTCA</b> 6	GGCTCAGATT CCGAGTCTAA	06	A AGCTTGCTTC F TCGAACGAAG	150 GGAGGGGGAT CCTCCCCCTA	210 GGGGACCTTC CCCCTGGAAG	270 TAACGGCTCA ATTGCCGAGT	330 ACTGAGACAC TGACTCTGTG
	20 GTTTGATCCT	GTTTGATCAT	80	AACAGGAAG/ TTGTCCTTC1	140 ACTGCCTGAT TGACGGACTA	200 GACCAAAGAG CTGGTTTCTC	260 GTAGGTGGGG CATCCACCCC	320 CCACACTGGA GGTGTGACCT
	10 AGA		20	GTCGAACGGT CAGCTTGCCA	130 TGTCTGGGAA ACAGACCCTT	190 AACGTCGCAA TTGCAGCGTT	250 GGATTAGCTA CCTAATCGAT	310 GGATGACCAG CCTACTGGTC

FIG. 8



i .

600 TGTTAAGTCA ACAATTCAGT GAACTCAGAG GAGGAATACC CTCCTTATGG CTCCTTATGG CACCCCTCGT	590 GCAGGCGGTT CGTCCGCCAAG ATGACCGTTC ATGAGATCTC ATCTCTAGAC GTGCGAAAGC CACGCTTTCG	580 TAAAGCGCAC ATTTCGCGTG GACGTAGACT GACGTAGACT CACTTTACGC CACTTTACGC CACTTTACGC CACTTTACGC ACTGCGAGTC ACTGCGAGTC ACTGCGAGTC ACTGCGAGTC		560 TTAATCGGAA AATTAGCCTT GGGCCCGAG GGGGCCCGAG CATCTTAAGG CATCTTAAGG CATCTTAAGG
66	650	640	630	620
TCT	TGGCAAG	CTGCATCTGA	AACCTGGGAA	CCCGGGCTC
AGA	ACCGTTC	GACGTAGACT	TTGGACCCTT	GGGCCCGAG
50	590	58	57	560
TC	AGGCGGTT	GCA	TTACTGGGC	TAATCGGAA
AG	TCCGCCAA	CGT	AATGACCCG	ATTAGCCTT
540	530	CTCCGTG	510	500
TAATACGGAG	GCAGCCGCGG		CACCGGCTAA	GCAGAAGAAG
ATTATGCCTC	CGTCGGCGCC		GTGGCCGATT	CGTCTTCTTC
480	470	460	450	440
TTTGCTCATT	AGTTAATACC	AAGGGAGTAA	AGCGGGGAGG	AAGTACTTTC
AAACGAGTAA	TCAATTATGG	TTCCCTCATT	TCGCCCTCC	TTCATGAAAG
420 AAGAAGGCCT TTCTTCCGGA	CGCGTGTATG		CAAGCCTGAT GTTCGGACTA	ACAATGGGCG TGTTACCCGC

## FIG. 88B

.



A.	MR 1 9 2004

	840 AGGTTGTGCC TCCAACACGG	900 TACGGCCGCA ATGCCGGCGT	960 GTGGTTTAAT CACCAAATTA	1020 CAGAGATGAG GTCTCTACTC	1080 CGTGTTGTGA GCACAACACT	1140	GCGGTCCGGC CGCCAGGCCG	1200 ACGTCAAGTC	ACGTCAAGIC ACGTCAAGTC TGCAGTTCAG
	830 GTCGACTTGG CAGCTGAACC	890 GCCTGGGGAG CGGACCCCTC	950 GGTGGAGCAT CCACCTCGTA	1010 CGGAAGTTTT GCCTTCAAAA	1070 GTCGTCAGCT CAGCAGTCGA	1130	TTTGTTGCCA AAACAACGGT		ATG GGTGGGG <u>ATG</u> CCACCCCTAC
	820 CGTAAACGAT GCATTTGCTA	880 TAAGTCGACC ATTCAGCTGG	940 CCGCACAAGC GGCGTGTTCG	1000 TTGACATCCA AACTGTAGGT	1060 CTGCATGGCT GACGTACCGA	1120 ACCC	ACCCTTATCC TGGGAATAGG	1180	ACTGGAGGAA TGACCTCCTT
•	810 TAGTCCACGC ATCAGGTGCG	870 GCTAACGCGT CGATTGCGCA	930 TGACGGGGGC ACTGCCCCCG	990 TTACCTGGTC AATGGACCAG	1050 GAGACAGGTG CTCTGTCCAC	1110 AACGAGCGCA	AACGAGCGCA TTGCTCGCGT	1170	CCAGTGATAA GGTCACTATT
	800 GATACCCTGG CTATGGGACC	860 GGCTTCCGGA CCGAAGGCCT	920 TCAAATGAAT AGTTTACTTA	980 GCGAAGÄACC CGCTTCTTGG	1040 CGGGAACCGT GCCCTTGGCA	1100 GC	TAAGTCCCGC ATTCAGGGCG	1160	AAGGAGACTG TTCCTCTGAC
	790 AACAGGATTA TTGTCCTAAT	850 CTTGAGGCGT GAACTCCGCA	910 AGGTTAAAAC TCCAATTTTG	970 TCGATGCAAC AGCTACGTTG	1030 AATGTGCCTT TTACACGGAA	1090	AATGTTGGGT T.TACAACCCA	1150	CGGGAACTCA GCCCTTGAGT

SB-3 SB-4

1260	AAGAGAAGCG TTCTCTTCGC	1320 AGTCTGCAAC TCAGACGTTG	1380 GTGAATACGT CACTTAIGCA CACTTAIGCA	1440 AGAAGTAGGT TCTTCATCCA	1500 GAAGTCGTAA CTTCAGCATT	
1250	GGCGCATACA	1310 TCCGGATTGG AGGCCTAACC	1370 GAATGCCACG CTTACGGTGC GC	1430 GGGTTGCAAA CCCAACGTTT	1490 TGACTGGGGT ACTGACCCCA	1550 TA
1240	GTGCTACAAT CACGATGTTA	1300 TGCGTCGTAG ACGCAGCATC	1360 TCGTGGATCA AGCACCTAGT	1420 CCATGGGAGT GGTACCCTCA	1480 TTGTGATTCA AACACTAAGT	1540 ATCACCTCCT TAGTGGAGGA
1230	GGCTACACAC	1290 CCTCATAAAG GGAGTATTTC	1350 TCGCTAGTAA AGCGATCATT	1410 GCCCGTCACA CGGCAGTGT	1470 GCTTACCACT CGAATGGTGA	1530 CTGCGGTTGG GACGCCAACC
1220 TTA	TTACGA TTACGACCAG AATGCTGGTC	1280 AGCAAGCGGA TCGTTCGCCT	1340 GAAGTCGGAA CTTCAGCCTT	1400 TGTACACACC ACATGTGTGG	1460 TCGGGAGGGC AGCCCTCCCG	1520 GTAGGGGAAC CATCCCCTTG
1210	ATCATGGCCC ATCATGGCCC ATCATGGCCC	1270 ACCTCGCGAG TGGAGCGCTC	1330 TCGACTCCAT AGCTGAGGTA	1390 TCCGGGCCT AGGGCCCGGA AGGGCCCGGA	1450 AGCTTAACCT TCGAATTGGA	1510 CAAGGTAACC GTTCCATTGG

1743

1743

FIG. 88D



ID NO:151) (SEQ ID NO:158)0AAATTGAAGAGTTTGATCATGGCTCAGATTGAACGCTGGCGGCAGGCCTAACACATGCA (SEQ ID NO:159)0 ~TTTTTATGGAGAGTTTGATCCTGGCTCAGAGTGAACGCTGGCGGCGTGCCTAATACATGCAGGCAG	GGCGGACGGG  60 AGTCGAACGGTAACAG GAAGAAGCTTGCTTCTTT GCTGACGAGTGGCGGGGGGGGGGGGGGGGGGGGGGGGGG	TGAGTAA 114 TGAGTAATGTCTGGGA_AACTGCCTGATGGAGGGGGGATAACTACTGGAAACGGTAGCTAATA 114 TGAGTAAGGTATAATCTGCCCTACACAAGAGGGACAACAGTTGGAAACGACTGCTAATA 113 TGAGTAACACGTGGATAACCTACCTATAAGACTGGGATAACTTCGGGAAACCGGAGCTAATA	175 CCGCATAACGTCGCAAGACCAAAGAGGGGGGCCTTCG-GGCCTTTG-GGGGGGGGGG	221 CCATCGGATGTGCCCAGATGGGATTAGCTAGTAGGTGGGGTAACGGCTCACCTAGGCGACGA 221 GTGTAGGATGAGACTATATAGTATCAGCTAGTTGGTAAGGTAATGGCTTACCAAGGCTATGA 229 CTTATAGATGGATCCGCGCTGCATTAGCTAGTTGGTAGGTA	283 TCCCTAGCTGGTCTGAGAGGATGACCAGCCACACTGGAACTGAGACACGGTCCAGACTCCTA 283 CGCTTAACTGGTCTGAGAGGATGATCAGTCACACTGGAACTGAGACAGGGTCCAGACTCCTA 291 TACGTAGCCGACCTGAGAGGGTGATCGGCCACACTGGAACTGAGACACGGTCCAGACTCCTA ACTCCTA
1638 (SEQ ] E.colirrsE Cam.jejun5 Stp.aureus	ER10 (SEQ ) E.colirrsE Cam.jejunS Stp.aureus	E.colirrsE Cam.jejun5 Stp.aureus	E.colirrsE Cam.jejun5 Stp.aureus	E.colirrsE Cam.jejun5 Stp.aureus	E.colirrsE Cam.jejun5 Stp.aureus 1659(COMPL)

FIG. 89A



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345 345 353

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CGGGAGGCAGTGGGGAATATTGCACAATGGGCGCAAGCCTGATGCAGCCATGCCGCGTG CGGGAGGCAGCAGTAGGGAATATTGCGCAATGGGGGAAACCCTGACGCAGCAACGCGGTG CGGGAGGCAGCAGTAGGGAATCTTCCGCAATGGGCGAAAGCCTGACGGAGCAACGCGGGTG CGGGAGGCAGCAG

468 455 476



GCACGCAGGCGGTTT GCGCGTAGGCGGATT GCGCGTAGGCGGGTTT GAGTCTCGTAGAGGGGGAATTCCAGGTGTAGCGGTGAATGCGTAGAGATCTGGAGGA GAGTGAGGGAGGCAGATGGAATTGGTGGTGTAGGGGGTAAATCCGTAGATATCACCAAGA GAGTGCAGAAGAGGGAAATTCCATGTGTAGCGGTGAATGCGCAGAGATATGGAGGA GCCCCCTGGACGAAGACTGACGCTCAGGTGCGAAAGCGTGGGGAGATCTGCTGGAACTGACGCTAAGGCGCGAAAGCGTGGGGAAGTTGTTCTGGTCTGACGCTTGACGCTTGATGTGCGAAAGCGTGGGGAA CCCGGGCTCAACCTGGAACTGCATCTGATACTGGCAAGCTT TAATGGCTTAACCATTAAACTGCTTGGGAAACTGATAGTCTA CCACGGCTCAACCGTGGAGGGTCATTGGAAACTGGAAAACTT CAAGCGTTAATCGGAATTACTGGGCGTAAAGCG CAAGCGTTACTCGGAATCACTGGGCGTAAAGGGG CAAGCGTTATCCGGAATTATTGGGCGTAAAGCG GTTAAGTCAGATGTGAAATC ATCAAGTCTCTTGTGAAATC TTTAAGTCTGATGTGAAAGC ATACCGGTGGCGAAGGCG ATACCCATTGCGAAGGCG ACACCAGTGGCGAAGGCG GTAATACGGAGGGTGC GTAATACGGAGGGTGC GTAATACGTAGGTGGC 0 9 8 2 8 0 9 7 4 407 53 300 90 4 6 2 5 5 5 5 99 7 /St jung **м** с м 5 8 **元** S rrs jun reu rrs jun reu rs un eu F - - - colii am.je; tp.aur li je au li je au .– Ф ⊐ **₽** am. tp-0 0 • • am tp oc. am tp U S C H  $\sim$   $\sim$ S C E S C E

FIG. 89C

TGGTAGTCCACGCCGTAAACGATGTCGACTTGGAGGTTGTGC TGGTAGTCCACGCCCTAAACGATGTACACTAGTTGTTGGGGT TGGTAGTCCACGCCGTAAACGATGAGTGCTAAGTGTTAGGGG

GCAAACAGGATTAGATAC GCAAACAGGATTAGATAC TCAAACAGGATTAGATAC

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0900) 1000) CGCCTGGGGAGTACGGC CGCCTGGGGAGTACGGT CGCCTGGGGAGTACGAC CCGGAGCTAACGCGTTAAGTCGACCATGCGAGCCATTAAGTGTACCACCATTAAGTGTACCATTAAGCACTCCATGCACTCCATTAAGCACTCCATGCACTCCA TT TA TG AG. 5 U F H H H (A) 1119 A F O TTG/ TAG TTC 0,0 0 8 14 4  $\infty \infty \infty$ **5** S  $\Box$ コ S ص <u>م</u> · D L e b · — @ 00 EO a t S C

AATTGACGGGGCCCGCACAAGCGGTGGAGCATGTGGTTTAATT AATAGACGGGGCCCGCACAAGCGGTGGAGCATGTGGTTTAATT AATTGACGGGGACCCGCACAAGCGGTGGAGCATGTGGGTTTAATT AGGTTAAAACTCAAATGA AGATTAAAACTCAAAGGA AGGTTGAAACTCAAAGGA AAA AA 9 0 0 000 **S** S rs un P 7 · — 7 e a • m .m @ 0 EO 4 E C

CTTACCTGGTCTTGACATCCACGGAAGTTTTCAGAGATGAGATCTTACCTGGGCTTGATATCCTAAGAACCTTTAGAGATAAGAGGCCTTACCAAACCTTTGACATTTGACATAGAGATAGAGCC GAAGAAC( GAAGAAC( GAAGAAC( CGATGCAACGCG CGAAGATACGCG CGAAGCAACGCG 7 80 1 73 999 **S** S rs un eu a D -**اب** و . . 0 EQ  $\mathcal{O}$ ٠ ه E S

TGA TGA TGA 17.6 17.6 17.6 10 H TCG. TCAGC TCAGC TCAGC CCGTGAGACAGGTGCTGCATGGCTGTCG CTTAGAGACAGGTGCTGCACGGCTGTCG CAAAGTGACAGGTGGTGCATGGTTGTCG FCGGG--AA-C FTGCTAGAA-C FCGGG--GGAC |---**|--|-**H U H 000 Ū Ā Ū I I I I I I I 6TG 6TG TTC 4 0 M 300 0 0 --- $m \sim c$ S  $\supset$  $\supset \Phi$ · — L j e au ---\_\_\_ 0 O EQ ٠ a + S C E

 $\cup$   $\cup$   $\vdash$ GCAACGAGCGCAACCC
GCAACGAGCGCTTATCTTTGTTGCCAGCGGTCCGG
GCAACGAGCGCAACCCACGTTTGTTGCTAACGGTTCGG
GCAACGAGCGCAACCCTTAAGTTGCTAACGGTTTAGG  $\mathcal{O}$  $\cup$   $\cup$ TGGGTTAAGTCC TGGGTTAAGTCC TGGGTTAAGTCC <del>-</del> <del>-</del> <del>-</del> -H H H AA GA GA コョフ 8 9 6 000 --**ш** с s rs un eu · F j e au • 70 Ú Ε  $\mathbf{Q}$  $\infty$ ٠ ه ٢ SUBS

FIG. 89D



ATGACGTCAAGTCATC
CAGTGATAAACTGGAGGAAGGTGGGGGATGACGTCAAGTCATC
CTTCG\_TAAGGAGGAGGAGGTGTGGGACGACGTCAAGTCATC  $\overline{C}$ T6. F F GA 6A GATTA CAAAGG/ CTAAAT/ CTAAGTI **⊢ ⊢** ⊢ 57) 54) 666AA( 6AGCA( 6GGCA( -....227 NO NO 127 127 151 ----0 Hm S S QQNEZ யயட J Q SSFINE **У** --- $\sigma$   $\supset$ <u>ں</u> م W 4 0 UEQ 1 1 8 ٠ **ه** + S C E S

TACAATGGCGCATACAAAGAGAAGCGACCT TACAATGGCATATAGAATGAGCGCAATAC TACAATGGACAATACAAAGGGCAGCGAAAC CAGGGCTACACACGTGC CAGGGGGACACACGTGC TTGGGCTACACACGTGC U U F <u>`</u> ∪ ⊢ **A** A O A 11 A T T A T T A T T A T T T A T T T A T T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T A T T T しつしつし 000  $\cup$   $\cup$   $\cup$   $\cup$ 0000 0000 **├ ├ ├ ├ ├ . . .** . <<<<<<4 8 4 0 0 1 7 7 -S 5 rs un eu · — ~ e D <u>ب</u> ه Ò  $\infty$  4 C Ε d  $\infty$ . a + SCES

1

TCATAAAGTGCGTCGTAGTCCGGATTGGAGTCTGCAACTCGACTC CTATAAAATATGTCCCAGTTCGGATTGTTCTCTGCAACTCGAGAG CCATAAAGTTGTTCTCAGTTCGGATTGTAGTCTGCAACTCGACTA CGGACCT - CAAAT( CAAATC( GAGAGCAAGC GAGGTGGAG-GAGGTCAAGC  $\cup$   $\cup$   $\cup$ 999 5 4 4 222 त्न स्न स्<del>न</del> m S S rrs un eu F . — F ب ص  $\supset$ · — @ 0 . . EO Ų . a + 

.666C .666T .666C 0 0 0A-ATGCCACGGTGAATACGTTC
CCATGCTACGGTGAATACGTTC
C-ATGCTACGGTGAATACGTTC
CGGTGAATACGTTC TAGTAATCGTGGATCAGA TAGTAATCGTAGATCAGC TAGTAATCGTAGATCAGC <u>ن</u> ن ن 909 CGGAATC( CGGAATC( TGGAATC(  $\vdash$   $\cup$   $\cup$ AAG AAG AAG 9 1 1 1 1 1 1 1 1 555 8 8 300 M M M日 S C rrs jun reu omp je au (c ٠,--0  $\cdot$   $\cdot$   $\infty$ am tp 74 1 S C E



CTA 6 6  $\mathcal{O} \cup \mathcal{O}$ ACT -- A  $\mathcal{O} \mathcal{O} \mathcal{O}$ ACTTTGTGATTCATGACTGGGGTGAAGTCGTAACAAGGTAA ACAGTGGAATCAGCGACTGGGGGTGAAGTCGTAACAAGGTAA AAGGTGGGACAAATGATTGGGGGGGGAAGTCGTAACAAGGTAG GCAAAGAAGTAGGTAGCT TCACTCGAAGCCGGAATAC ACACCCGAAGCCGGTGGAG CACACCATGGGAGTGGGTTG CACACCATGGGAGTTGATTT CACACCACGAGAGTTTGTAA TTA T--TTT(  $\cup$   $\cup$   $\cup$ F F F GATCAC( GATCAC( GATCAC( .GGTTG( CGT CGT CGT 000  $\tilde{\mathbf{U}}$   $\tilde{\mathbf{U}}$   $\mathbf{U}$ CGT  $\cup$   $\cup$   $\cup$ 0 90 <u>ن</u> ب ت ت ت CG( TA( 5 1 1 2 1 3 1 CTTGTACACACC CTTGTACTCACC ATTGTACACACC AGGGGAACCT AGGAGAACCT ATCGGAAGGT 3-66A6666 ---T-AGTT FAGGAGCTA 5 1 AC, TAT UVAU  $0 \infty 0$ 25 エアュ 629 8 9 6 100  $\omega$ 444 5 4 5 -rrsE jun5 reus ompl rrsE jun5 reus sE n5 us - 2 a li je au (c ·- v = .- o ⊐ م ب و *اس ه* .co am. tp. · · m 0 am tp ат tр 74 **J** S C H S C S C

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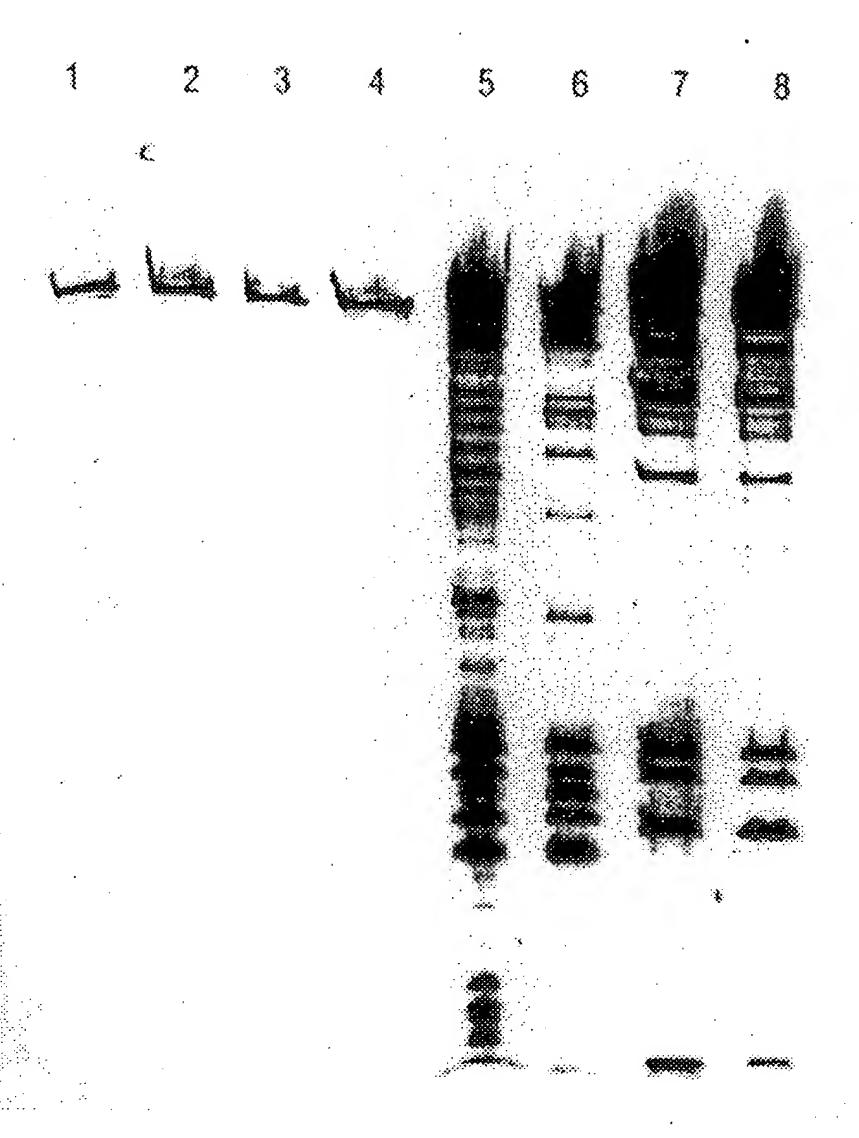


FIG. 90



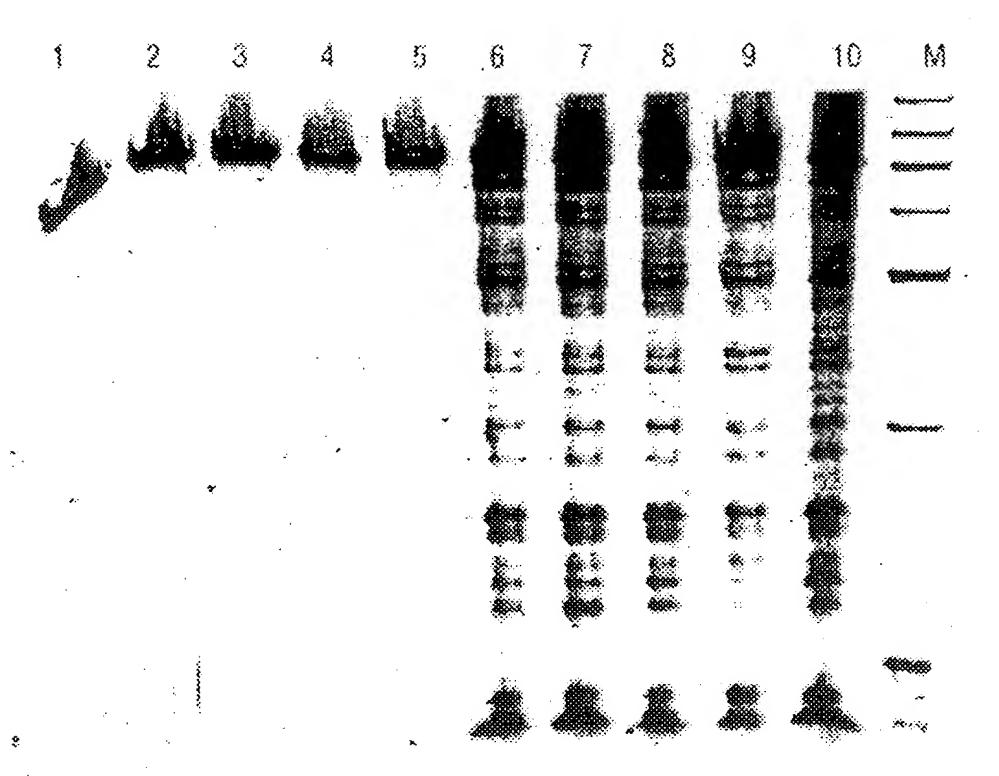


FIG. 91A

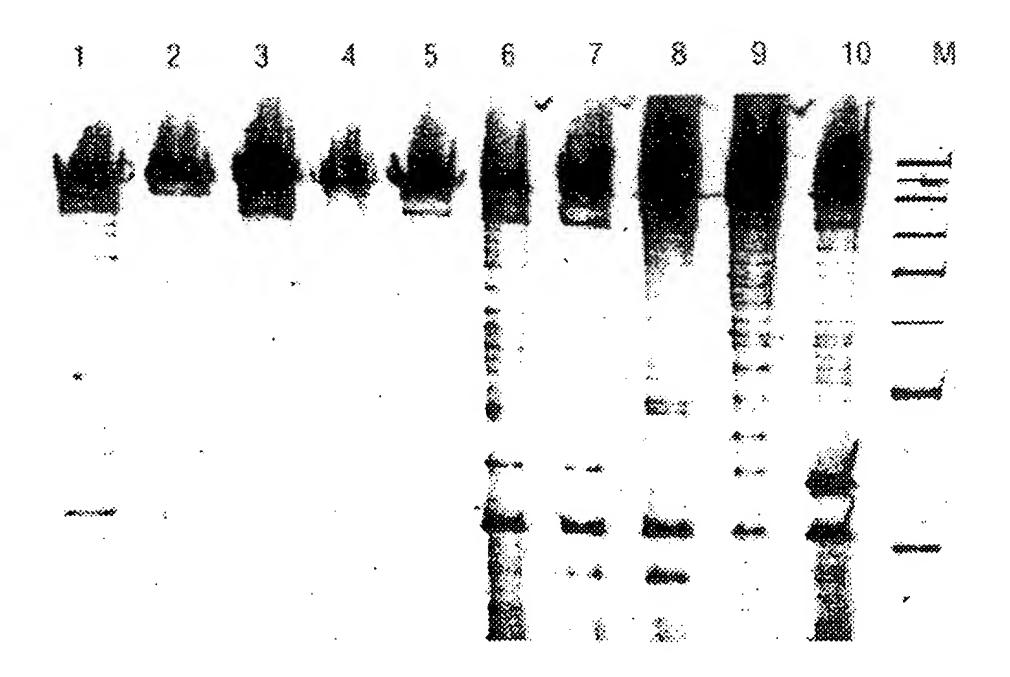


FIG. 91B



1 2 3

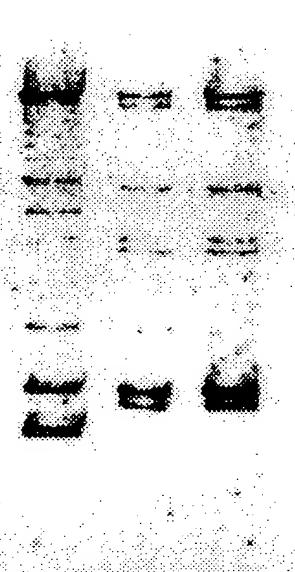


FIG. 92



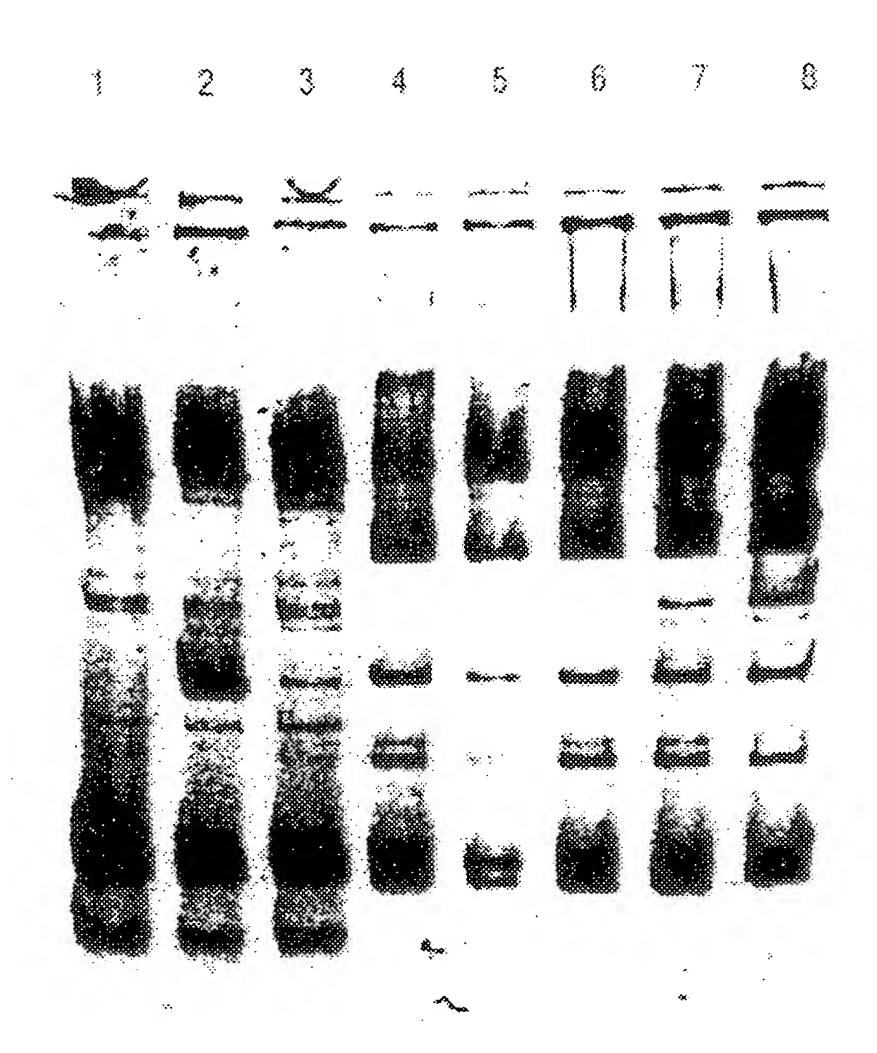


FIG. 93



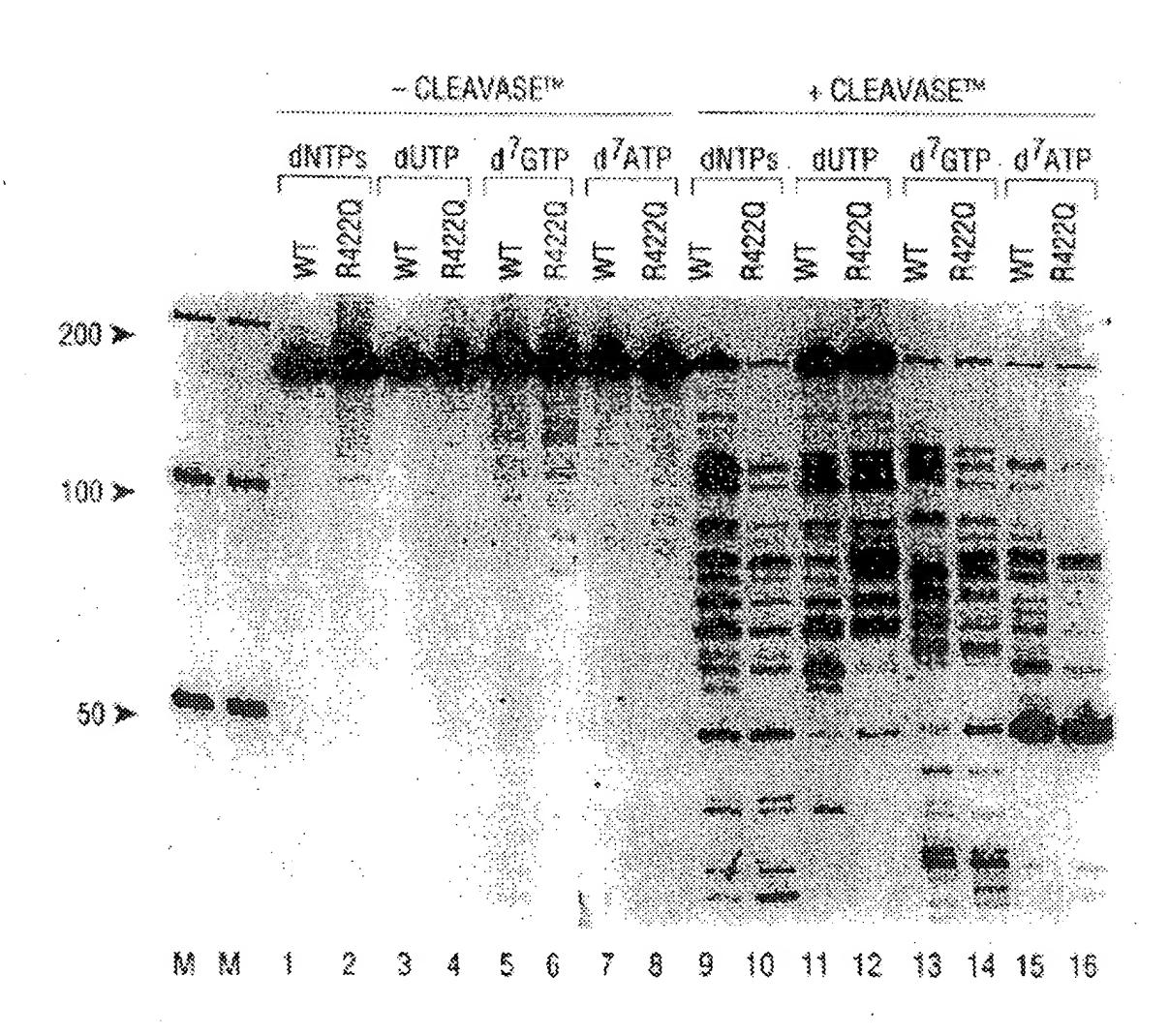


FIG. 94